

10/513699

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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAPplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAPplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAPplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAPplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAPplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAPplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new

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custom IPC display formats
NEWS 32 JAN 28 MARPAT searching enhanced
NEWS 33 JAN 28 USGENE now provides USPTO sequence data within 3 days
of publication
NEWS 34 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 35 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements
NEWS 36 FEB 08 STN Express, Version 8.3, now available
NEWS 37 FEB 20 PCI now available as a replacement to DPCI

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 20:25:33 ON 22 FEB 2008

=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 20:25:48 ON 22 FEB 2008
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STRUCTURE FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9
DICTIONARY FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9
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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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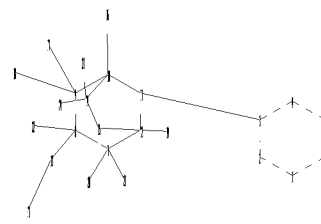
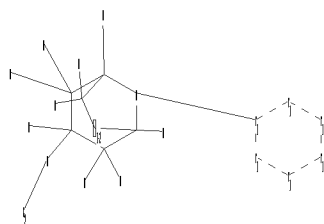
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

10/513699

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10518114allow.str



chain nodes :
13 16 17 18 19 20 21 22 23 24 31
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 14 15
chain bonds :
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ring bonds :
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14-15
exact/norm bonds :
1-2 1-6 2-3 3-4 3-11 4-5 5-6 7-8 7-12 7-20 7-21 8-9 8-13 8-22 9-10
9-17 9-18 10-11 10-14 10-16 11-12 12-15 12-19 13-31 14-15 14-23 14-24
isolated ring systems :
containing 1 : 7 :

G1:C,N

G2:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 31:CLASS

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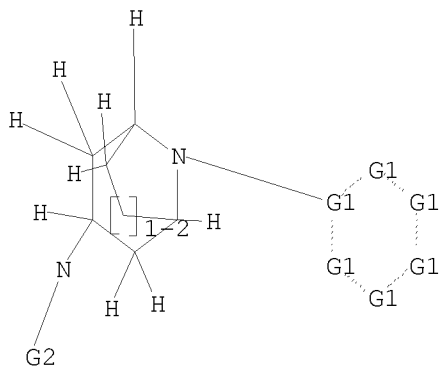
10/513699

L1 STRUCTURE UPLOADED

$$\Rightarrow d_{11}$$

L1 HAS NO ANSWERS

L1	STR
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G1 C, N

G2 C, H

Structure attributes must be viewed using STN Express query preparation.

=> s ll full

FULL SEARCH INITIATED 20:26:47 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 110328 TO ITERATE

100.0% PROCESSED 110328 ITERATIONS

214 ANSWERS

SEARCH TIME: 00.00.01

L2 214 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

178.82

179.03

FILE 'CAPLUS' ENTERED AT 20:26:52 ON 22 FEB 2008

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FILE LAST UPDATED: 21 Feb 2008 (20080221/ED)

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=> s 12 full
L3 19 L2

=> d ibib abs hitstr tot

L3 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:757385 CAPLUS

DOCUMENT NUMBER: 147:166304

TITLE: Preparation of heterocyclic compounds as janus kinase 3 inhibitors

INVENTOR(S): Inoue, Takayuki; Tanaka, Akira; Nakai, Kazuo; Sasaki, Hiroshi; Takahashi, Fumie; Shirakami, Shohei; Hatanaka, Keiko; Nakajima, Yutaka; Mukoyoshi, Koichiro; Hamaguchi, Hisao; Kunikawa, Shigeki; Higashi, Yasuyuki

PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan

SOURCE: PCT Int. Appl., 266pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007077949	A1	20070712	WO 2006-JP326327	20061225
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:

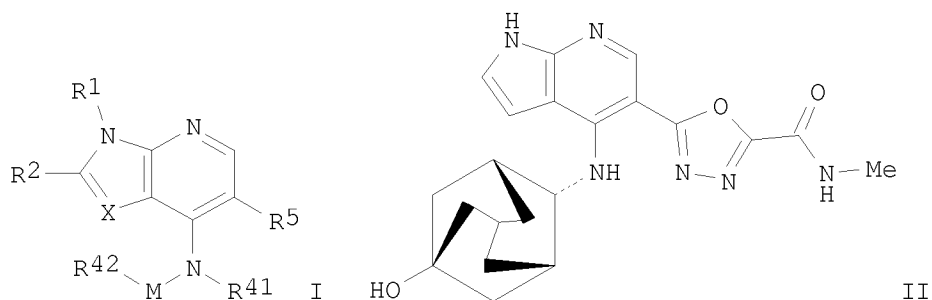
JP 2005-378858

A 20051228

OTHER SOURCE(S):

MARPAT 147:166304

GI



AB The title heterocyclic compds. I [wherein X = N or (un)substituted CH; M = a bond or CH₂; R¹ and R² = independently H or (un)substituted alkyl; R⁴¹ = H or (un)substituted heteroaryl; R⁴² = an (un)substituted bridged ring

group; R5 = halo, CN, acyl, etc.; or R41 and R5 form a ring.] or pharmaceutically acceptable salts thereof were prepared as janus kinase 3 (JAK3) inhibitors. For example, II was prepared in a multi-step synthesis. The compds. are useful for treating or preventing various immune diseases, such as rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, etc.

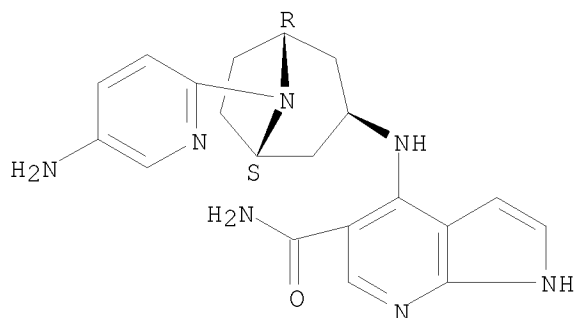
IT 944117-13-9P 944122-15-0P 944122-18-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944117-13-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-amino-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

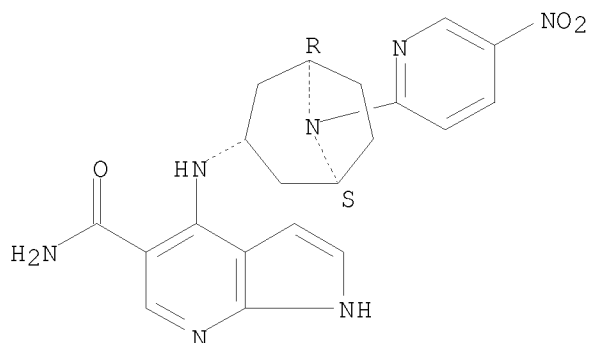
Relative stereochemistry.



RN 944122-15-0 CAPLUS

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Relative stereochemistry.

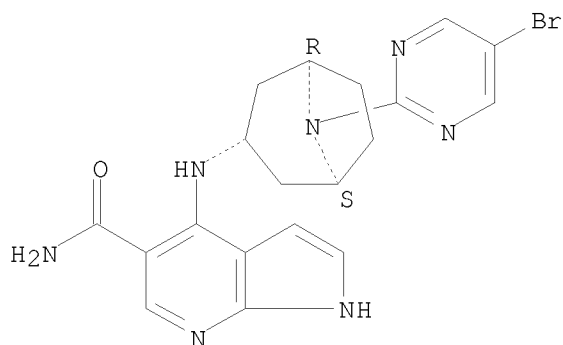


RN 944122-18-3 CAPLUS

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Relative stereochemistry.

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IT 944117-21-9P 944117-22-0P 944117-26-4P
944117-44-6P 944117-52-6P 944118-18-7P
944118-20-1P 944118-46-1P 944121-64-6P
944121-87-3P 944121-88-4P 944121-89-5P
944121-90-8P 944121-91-9P 944121-93-1P
944121-94-2P 944121-98-6P 944122-13-8P
944122-14-9P 944122-16-1P 944122-17-2P
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944122-25-2P 944122-26-3P 944122-28-5P
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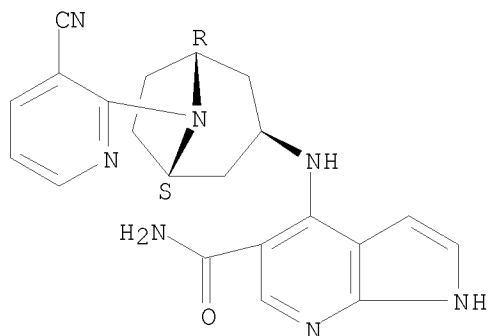
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944117-21-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(3-cyano-2-
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Relative stereochemistry.

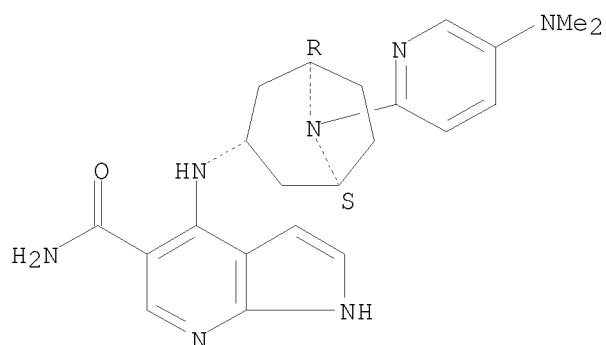


RN 944117-22-0 CAPLUS

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Relative stereochemistry.

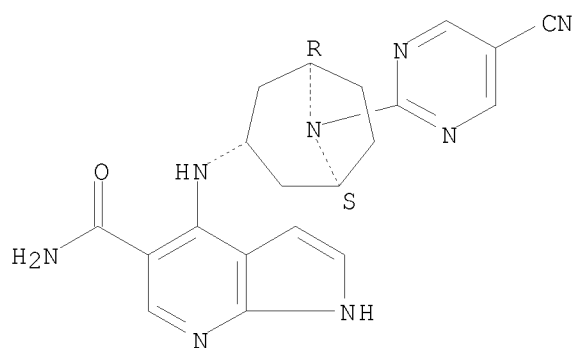
10/513699



RN 944117-26-4 CAPLUS

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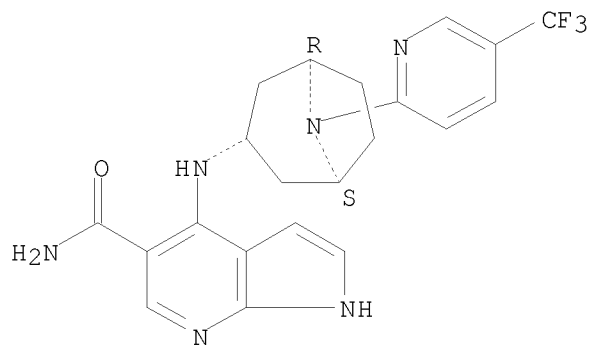
Relative stereochemistry.



RN 944117-44-6 CAPLUS

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Relative stereochemistry.



RN 944117-52-6 CAPLUS

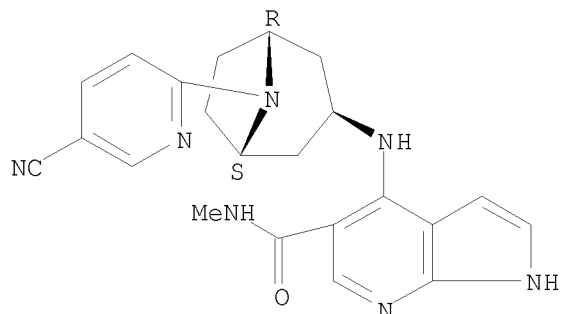
<12/04/2007>

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CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]-N-methyl- (CA INDEX NAME)

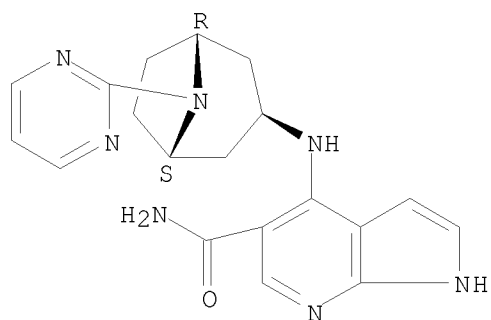
Relative stereochemistry.



RN 944118-18-7 CAPLUS

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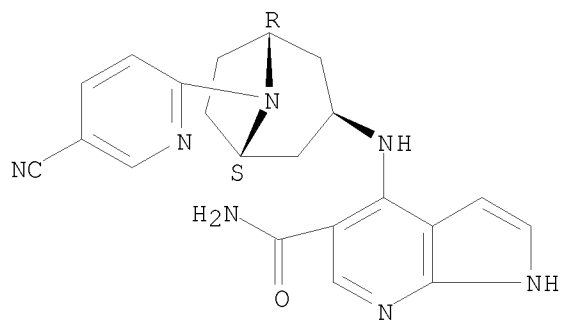
Relative stereochemistry.



RN 944118-20-1 CAPLUS

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Relative stereochemistry.



RN 944118-46-1 CAPLUS

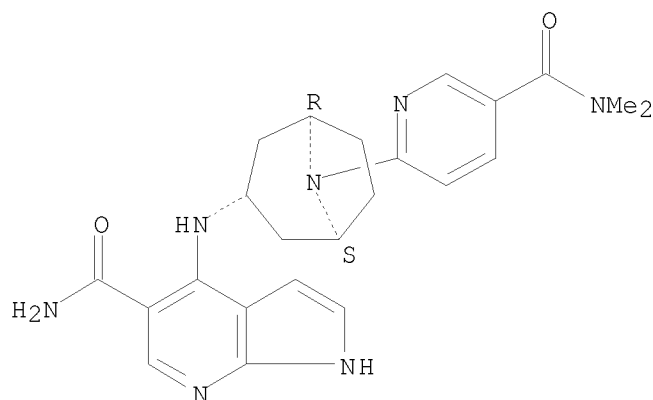
<12/04/2007>

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CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-
[(dimethylamino)carbonyl]-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]-
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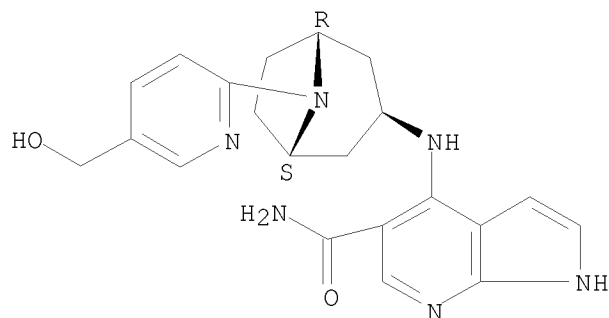
Relative stereochemistry.



RN 944121-64-6 CAPLUS

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2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

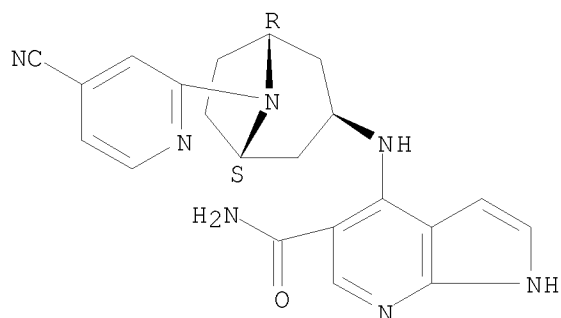


RN 944121-87-3 CAPLUS

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Relative stereochemistry.

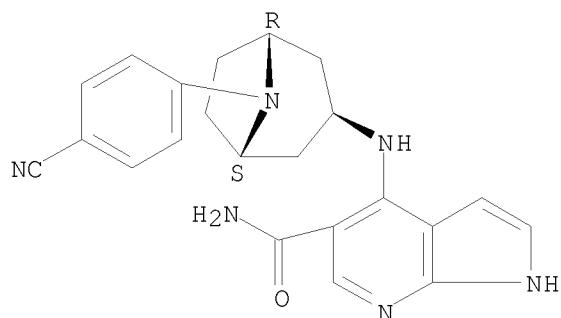
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RN 944121-88-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[3-exo)-8-(4-cyanophenyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

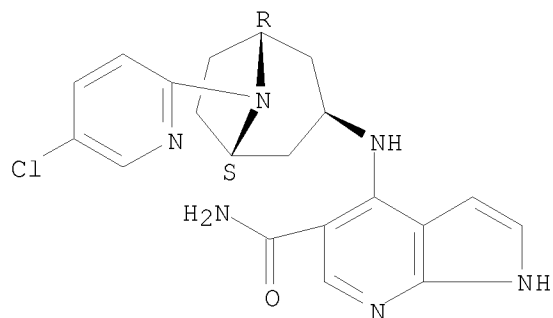
Relative stereochemistry.



RN 944121-89-5 CAPLUS

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Relative stereochemistry.

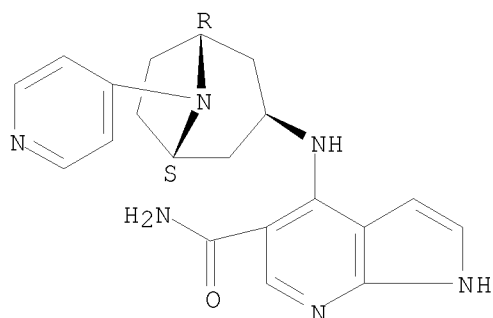


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Relative stereochemistry.

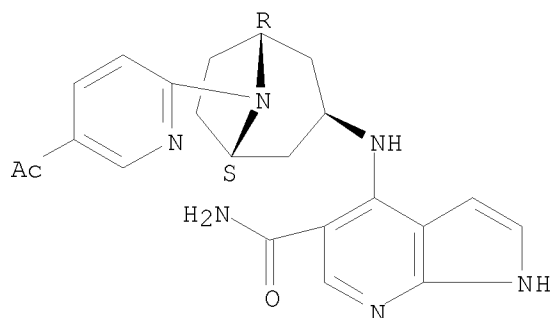
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RN 944121-91-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[(3-exo)-8-(5-acetyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944121-93-1 CAPLUS

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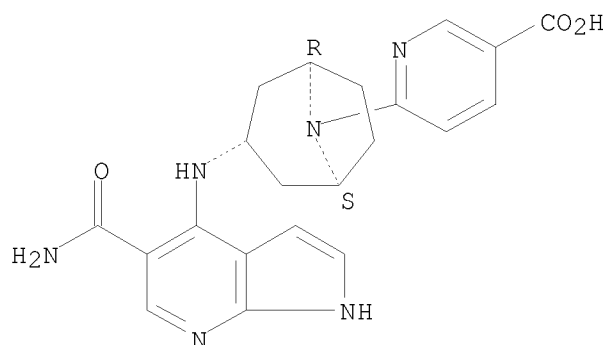
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Relative stereochemistry.

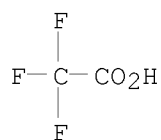
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CM 2

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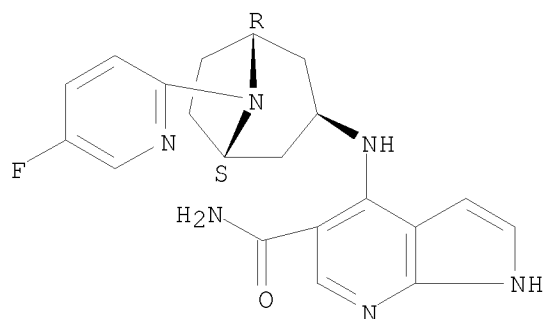
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Relative stereochemistry.

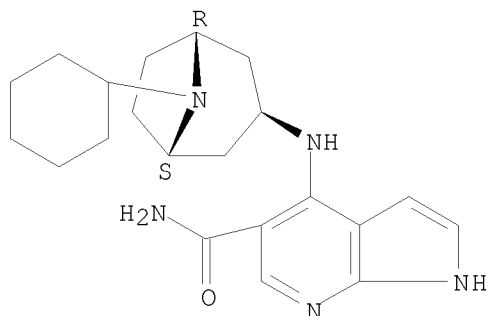


RN 944121-98-6 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

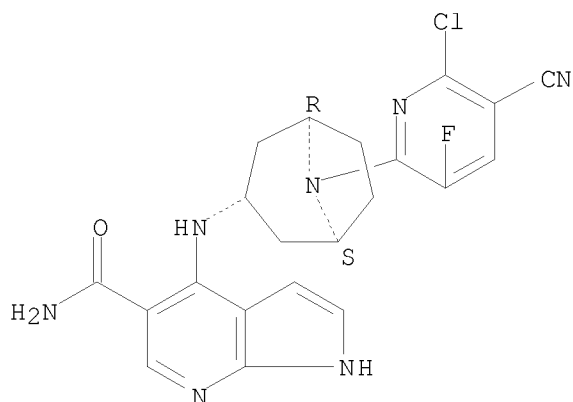
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RN 944122-13-8 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[(3-exo)-8-(6-chloro-5-cyano-3-fluoro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

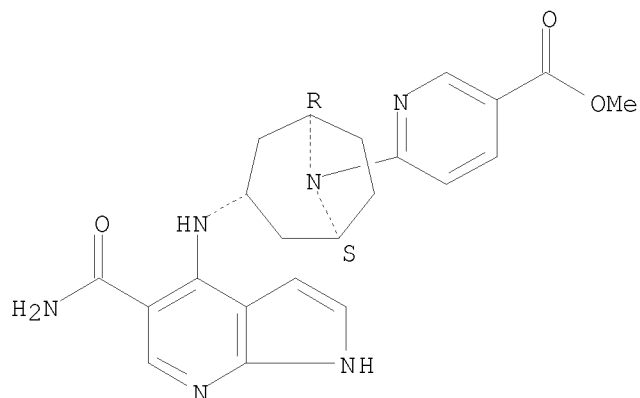


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CN 3-Pyridinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

Relative stereochemistry.

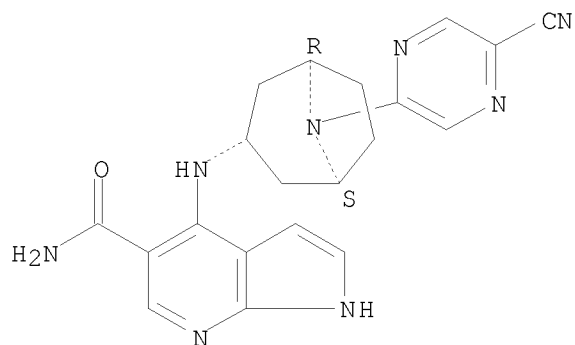
10/513699



RN 944122-16-1 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-cyano-2-pyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

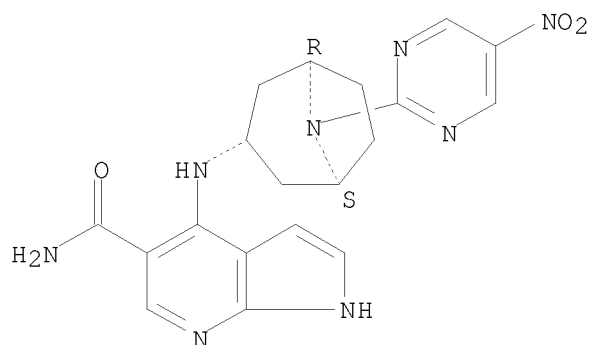
Relative stereochemistry.



RN 944122-17-2 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(5-nitro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

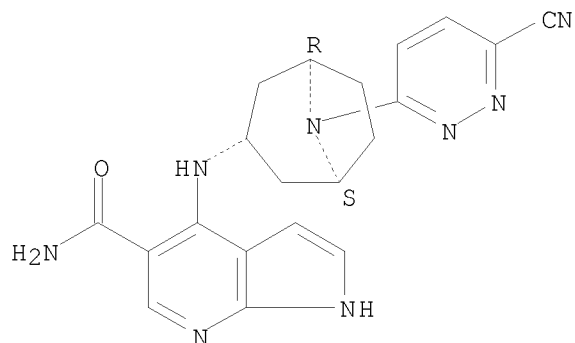
Erich Leese

10/513699

RN 944122-19-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

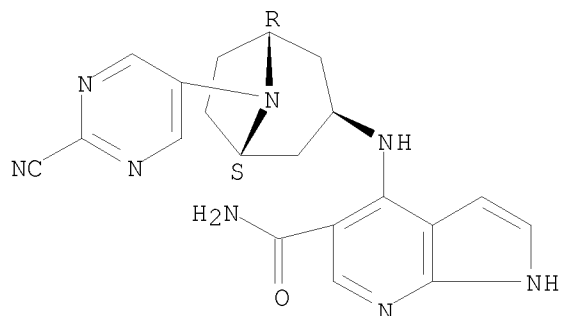
Relative stereochemistry.



RN 944122-21-8 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(2-cyano-5-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

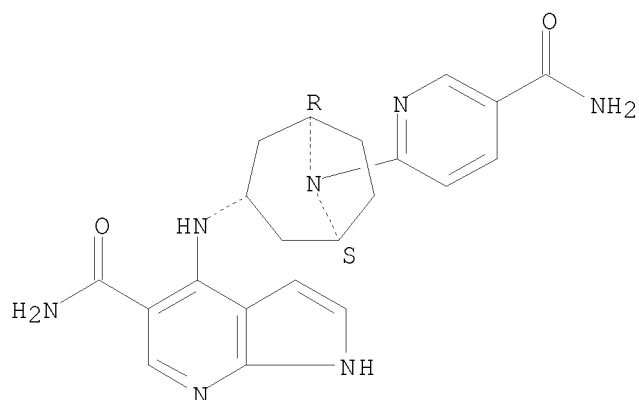


RN 944122-23-0 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[5-(aminocarbonyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

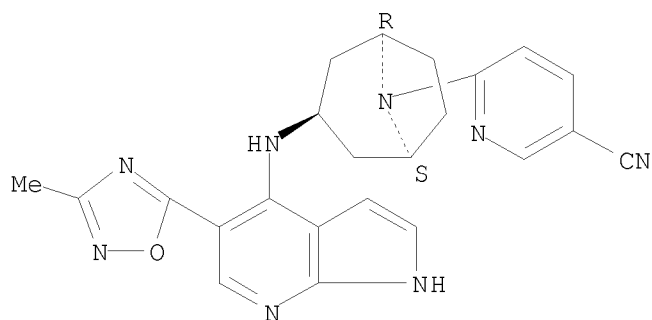
10/513699



RN 944122-25-2 CAPLUS

CN 3-Pyridinecarboxamide, 6-[(3-endo)-3-[[5-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

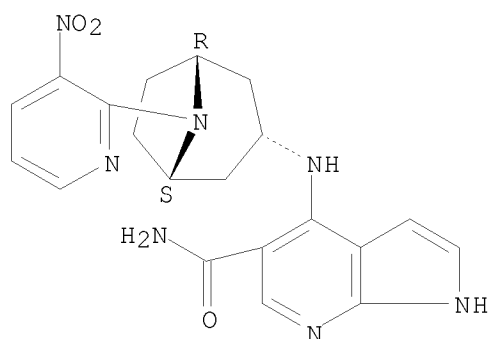
Relative stereochemistry.



RN 944122-26-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[(3-endo)-8-(3-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

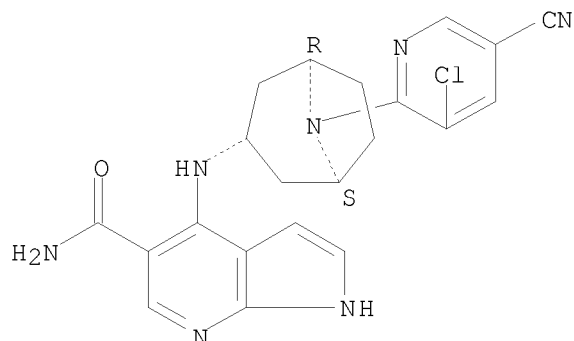
Erich Leese

10/513699

RN 944122-28-5 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-(3-chloro-5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

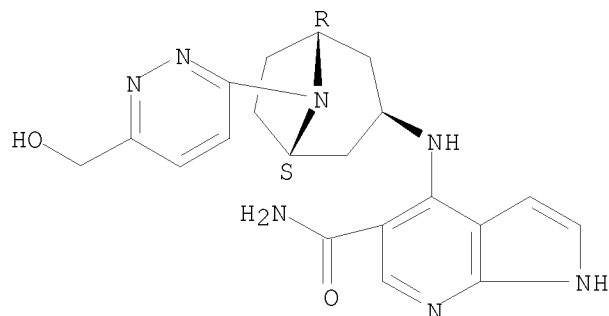
Relative stereochemistry.



RN 944122-29-6 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-exo)-8-[6-(hydroxymethyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.

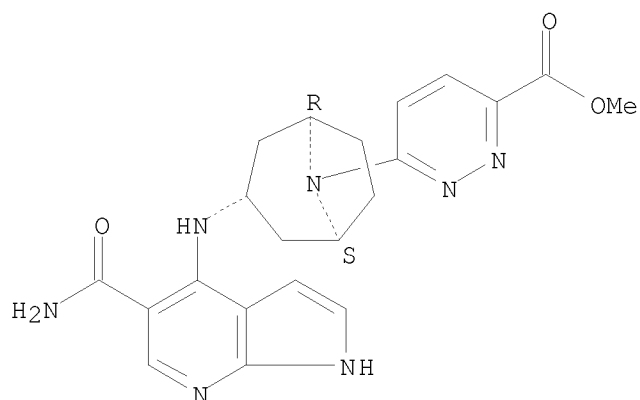


RN 944122-31-0 CAPLUS

CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

Relative stereochemistry.

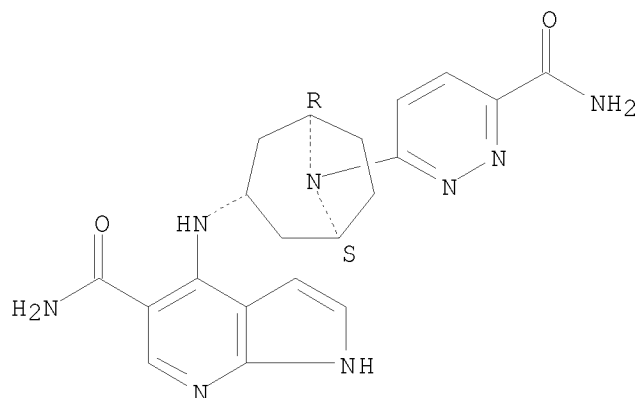
10/513699



RN 944122-32-1 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[3-exo)-8-[6-(aminocarbonyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

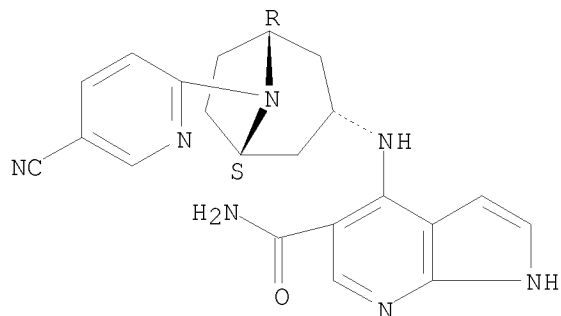
Relative stereochemistry.



RN 944135-23-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

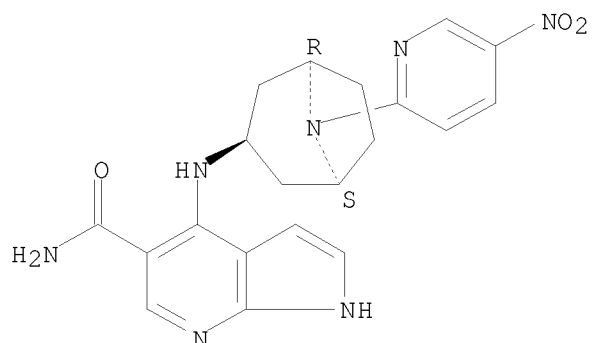
Erich Leese

10/513699

RN 944135-24-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

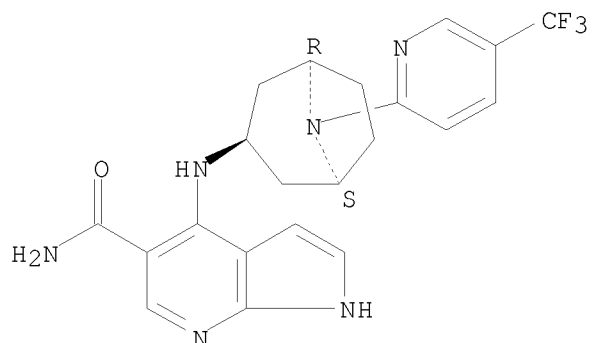
Relative stereochemistry.



RN 944135-25-5 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[(3-endo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



IT 944122-57-0P 944123-89-1P

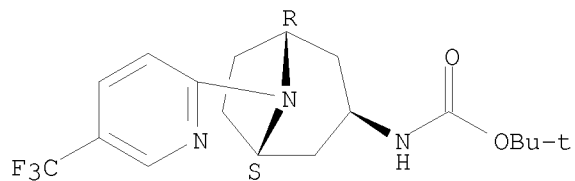
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944122-57-0 CAPLUS

CN Carbamic acid, N-[(3-exo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Relative stereochemistry.

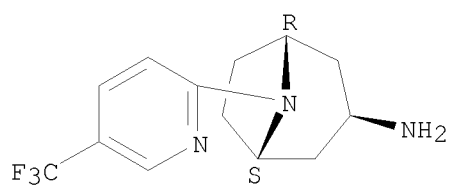
10/513699



RN 944123-89-1 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[5-(trifluoromethyl)-2-pyridinyl]-,
(3-exo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/513699

L3 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:409606 CAPLUS

DOCUMENT NUMBER: 146:401834

TITLE: Preparation of azabicyclo[2.2.1]octane derivatives as pesticides

INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio; Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao

PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan

SOURCE: PCT Int. Appl., 97pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

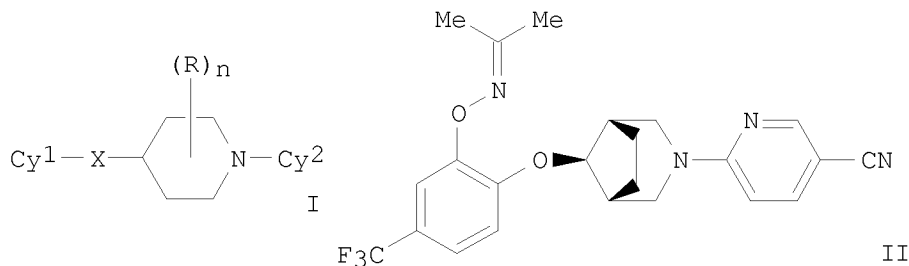
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007040280	A1	20070412	WO 2006-JP320126	20061006
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.:

JP 2005-294126	A	20051006
JP 2005-294127	A	20051006
JP 2005-297803	A	20051012
JP 2005-297804	A	20051012
JP 2006-16877	A	20060125
JP 2006-182314	A	20060630

OTHER SOURCE(S): MARPAT 146:401834

GI



AB The title compds. I [wherein Cy1 = (un)substituted heterocyclyl; Cy2 = (un)substituted cyclyl, heterocyclyl, etc.; n = 0-9; X = O, S, SO₂, or (un)substituted NH; R = OH, halo, (un)substituted NH₂, etc.; or two R's

<12/04/2007>

Erich Leese

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form a ring] are prepared as pest control agents. For example, the compound II was prepared in a multi-step synthesis. Some of compds. I showed excellent pesticidal activities in tests.

IT 933797-20-7P 933797-68-3P 933797-69-4P
933797-70-7P 933797-71-8P

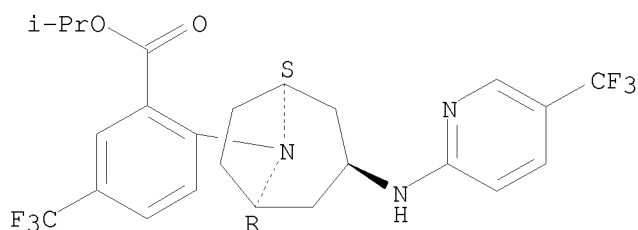
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pesticide; preparation of azabicyclo[2.2.1]octane derivs. as pesticides)

RN 933797-20-7 CAPLUS

CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 1-methylethyl ester (CA INDEX NAME)

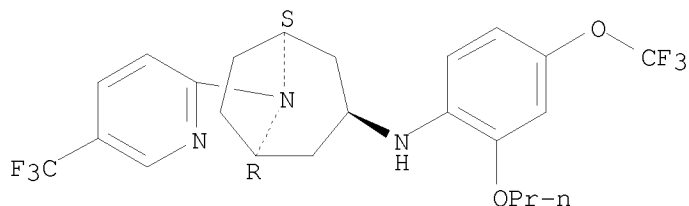
Relative stereochemistry.



RN 933797-68-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

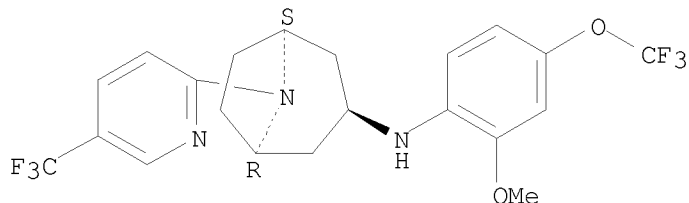
Relative stereochemistry.



RN 933797-69-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.

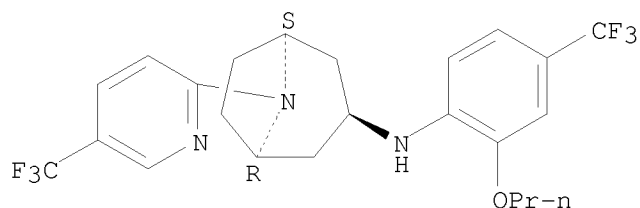


RN 933797-70-7 CAPLUS

10/513699

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-
8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

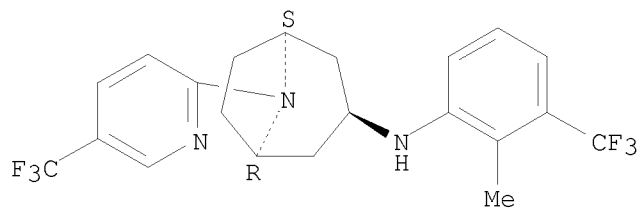
Relative stereochemistry.



RN 933797-71-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methyl-3-(trifluoromethyl)phenyl]-8-
[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

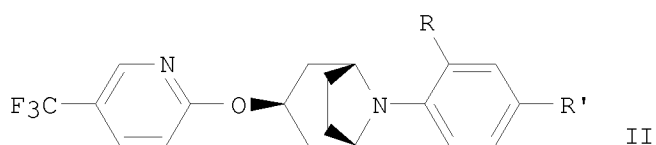
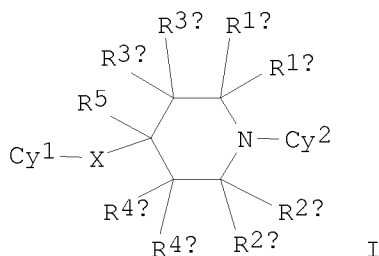
7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/513699

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:405401 CAPLUS
DOCUMENT NUMBER: 146:421857
TITLE: Preparation of bridged cyclic amine compounds as pest
control agents
INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio;
Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao
PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007040282	A1	20070412	WO 2006-JP320133	20061006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2005-294126	A 20051006
			JP 2005-294127	A 20051006
			JP 2005-297803	A 20051012
			JP 2005-297804	A 20051012
			JP 2006-16877	A 20060125
			JP 2006-182314	A 20060630
OTHER SOURCE(S):	MARPAT 146:421857			
GI				



AB Title compds. I [Cy1 = (un)substituted aromatic ring; X = oxygen, sulfur, (un)substituted nitrogen, etc.; R1a and R2a, R1a and R4a, R2a and R3a, or R3a and R4a may combine to form a saturated ring.; R1a-R4a, R1b-R4b and R5 = H, hydroxy, halo, etc.; Cy2 = (un)substituted aromatic ring; when R1a and R2a may combine to form a saturated ring and Cy1 is a (un)substituted Ph, Cy2 is a (un)substituted aromatic heterocycle.; when Cy1 is a (un)substituted Ph and Cy2 is a pyridin-2-yl, Cy2 is a pyridin-2-yl substituted with one or more cyano groups.], salts or N-oxides thereof were prepared For example, reaction of tropine with 2-chloro-5-trifluoromethylpyridine followed by treatment with 2,2,2-trichloroethyl chloroformate, reduction using Zn/acetic acid and O-arylation with 2-fluoro-5-trifluoromethylbenzaldehyde afforded compound II [R = CHO; R' = CF₃]. Compound II [R = OCH₂CH₂CH₃; R' = CF₃] controlled two-spotted spider mite by 100%.

IT 933797-20-7P 933797-68-3P 933797-69-4P

933797-70-7P 933797-71-8P

RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

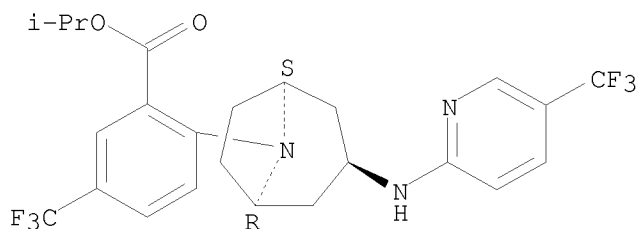
(preparation of bridged cyclic amine compds. as pest control agents)

RN 933797-20-7 CAPLUS

CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 1-methylethyl ester (CA INDEX NAME)

Relative stereochemistry.

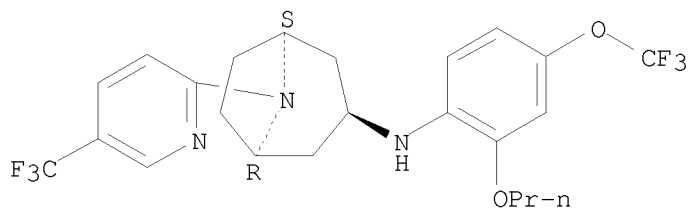
10/513699



RN 933797-68-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-
8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

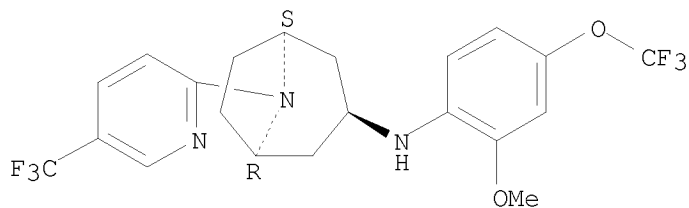
Relative stereochemistry.



RN 933797-69-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-
8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

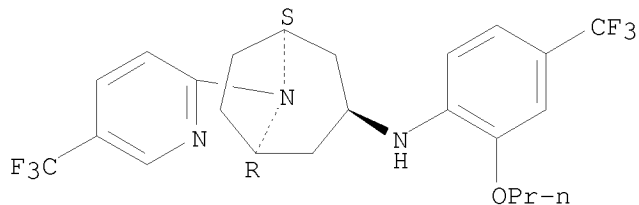
Relative stereochemistry.



RN 933797-70-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-
8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.

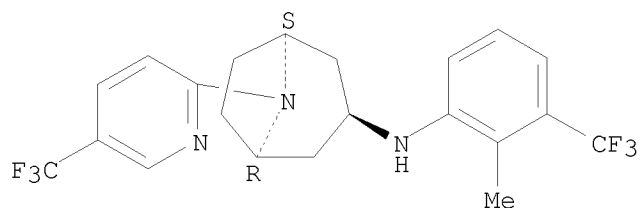


RN 933797-71-8 CAPLUS

10/513699

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methyl-3-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.

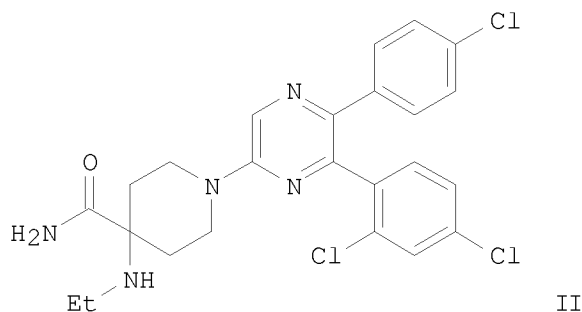
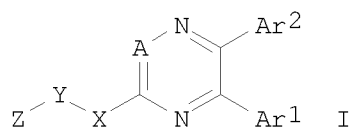


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/513699

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1124114 CAPLUS
DOCUMENT NUMBER: 145:455030
TITLE: Preparation of substituted heteroaryl CB1 antagonists
INVENTOR(S): Yuan, Jun; Guo, Qin; Zhao, He; Hu, Shaojing;
Whitehouse, Darren; Fringle, Wallace; Mao, Jianmin;
Maynard, George; Hammer, Jack; Wustrow, David; Li,
Hongbin
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 447pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2006113704	A2	20061026	WO 2006-US14548	20060418
WO 2006113704	A3	20070208		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2606288	A1	20061026	CA 2006-2606288	20060418
US 2007078135	A1	20070405	US 2006-406532	20060418
EP 1871762	A2	20080102	EP 2006-750555	20060418
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			US 2005-672452P	P 20050418
			WO 2006-US14548	W 20060418
OTHER SOURCE(S):	MARPAT 145:455030			
GI				



AB The title compds. I [A = CR₁ or N; Ar₁, Ar₂ = (un)substituted 5-10 membered carbocycle and heterocycle; X = (un)substituted CH₂, O, NH or SOmNH; m = 0-2; Y = (un)substituted alkylene; Z = (un)substituted OH, NH₂, SOmNH₂, etc.; R₁ = H, halo, CN, etc.] which may be used to modulate CB₁ activity in vivo or in vitro, and are particularly useful in the treatment of conditions responsive to CB₁ modulation in humans, domesticated companion animals and livestock animals, including appetite disorders, obesity and addictive disorders, were prepared E.g., a multi-step synthesis of II, starting from 2,6-dichloropyrazine and 4-(ethylamino)piperidine-4-carboxamide, was given. Exemplified compds. I were tested at CB₁ receptor. Thus, II as many other representative compds. I showed IC₅₀ of 2 μM or less. Pharmaceutical compns. and methods for using compds. I to treat disorders responsive to CB₁ modulation are provided, as are methods for using such ligands for receptor localization studies and various in vitro assays.

IT 913281-93-3P 913281-94-4P 913281-97-7P
913282-02-7P 913282-12-9P 913282-17-4P

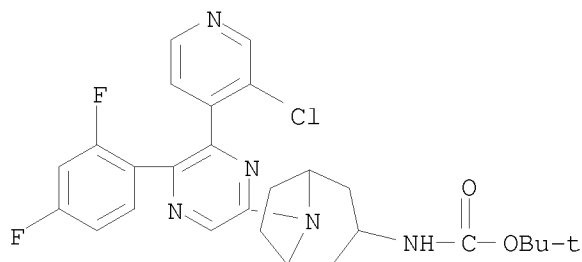
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted heteroaryl compds. useful in treatment of diseases responsive to CB₁ activation)

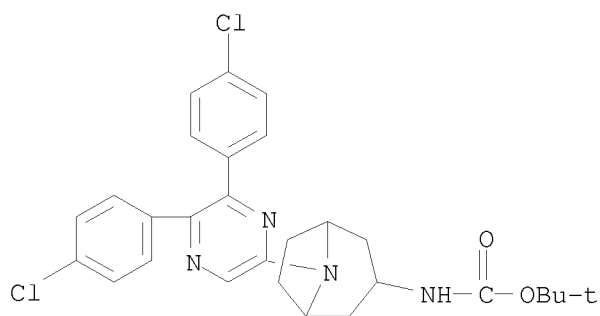
RN 913281-93-3 CAPLUS

CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

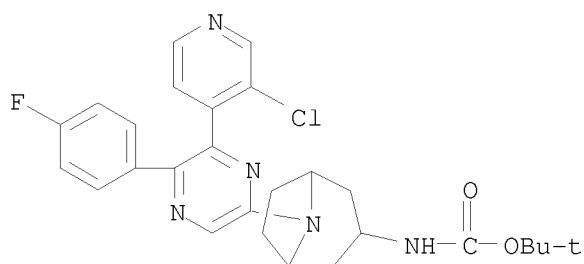
10/513699



RN 913281-94-4 CAPLUS
CN Carbamic acid, [8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

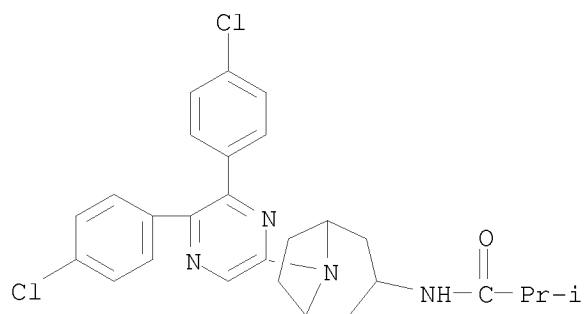


RN 913281-97-7 CAPLUS
CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



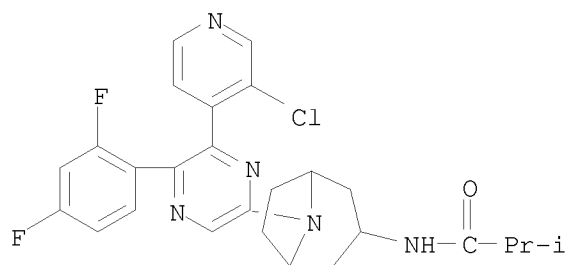
RN 913282-02-7 CAPLUS
CN Propanamide, N-[8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)

10/513699



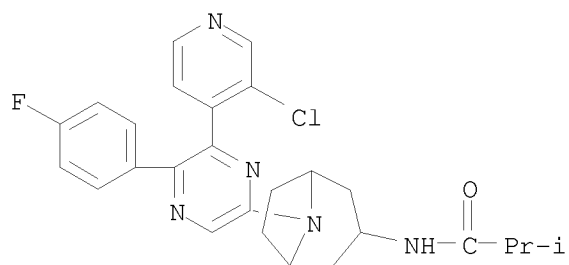
RN 913282-12-9 CAPLUS

CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI)
(CA INDEX NAME)



RN 913282-17-4 CAPLUS

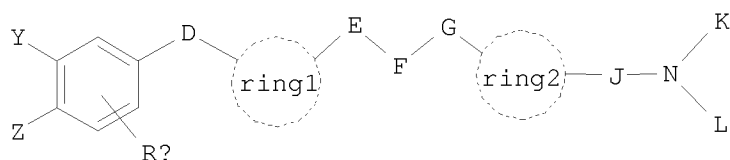
CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



10/513699

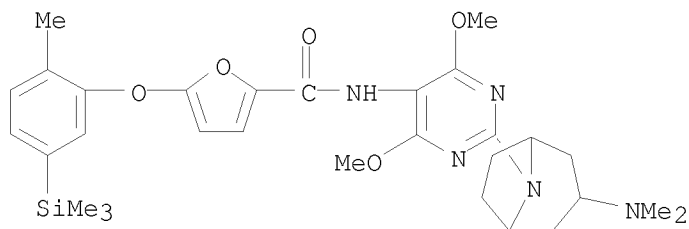
L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:606621 CAPLUS
DOCUMENT NUMBER: 145:63034
TITLE: Preparation of silicon compounds and their use in
medicament
INVENTOR(S): Showell, Graham Andrew; Walsh, Louise Marie; Mandal,
Ajay Kumar
PATENT ASSIGNEE(S): Paradigm Therapeutics Ltd., UK
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006064277	A1	20060622	WO 2005-GB4905	20051216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005315331	A1	20060622	AU 2005-315331	20051216
CA 2590881	A1	20060622	CA 2005-2590881	20051216
EP 1824863	A1	20070829	EP 2005-820647	20051216
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101107259	A	20080116	CN 2005-80043255	20051216
IN 2007DN03844	A	20070831	IN 2007-DN3844	20070522
KR 2007097468	A	20071004	KR 2007-714460	20070625
PRIORITY APPLN. INFO.:			GB 2004-27722	A 20041217
			WO 2005-GB4905	W 20051216
OTHER SOURCE(S):			CASREACT 145:63034; MARPAT 145:63034	
GI				



I

- AB Preparation of title compds., e.g. I (D = (un)substituted alkylene, O, thionyl, sulfonyl, etc.; E, F, G = same or different (un)substituted alkylene, (un)substituted amino, etc.; J = bond, heterocycloalkyl, etc.; K, L = same or different H, alkyl, cycloalkyl, alkoxy, etc.; Ra, K or L taken together as heterocycloalkyl; Ra = H, halo, alkyl, aryl, hydroxy, alkoxy, etc.; Y, Z = same or different H, halo, alkyl, hydroxy, alkoxy, cyano, organosilyl, etc.; ring1 and ring2 = same or different arylene, heteroarylene optionally substituted with Ra; at least one of Y and Z includes a Si atom), and their use in therapy is described.
- IT 891860-56-3P, 5-(2-Methyl-5-(trimethylsilyl)phenoxy)-N-(2-(3-(dimethylamino)-8-azabicyclo[3.2.1]octan-8-yl)-4,6-dimethoxypyrimidin-5-yl)furan-2-carboxamide
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of organosilyl compds. and their use in medicament)
- RN 891860-56-3 CAPLUS
- CN 2-Furancarboxamide, N-[2-[3-(dimethylamino)-8-azabicyclo[3.2.1]oct-8-yl]-4,6-dimethoxy-5-pyrimidinyl]-5-[2-methyl-5-(trimethylsilyl)phenoxy]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/513699

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1006982 CAPLUS

DOCUMENT NUMBER: 140:59518

TITLE: Preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]hetero cyclic carbonitriles as dipeptidyl-peptidase-IV inhibitors

INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori, Sandor; Boronkay, Eva; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos T.; Urban-Szabo, Katalin; Varga, Marton

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

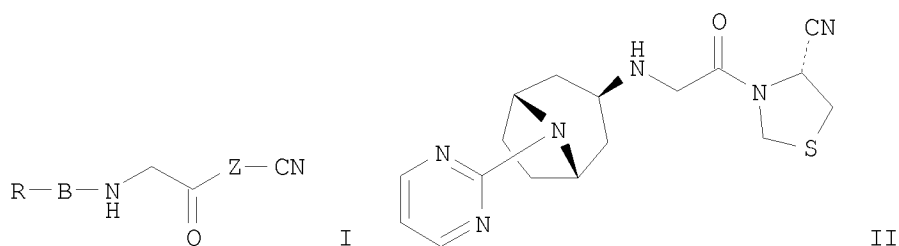
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106456	A2	20031224	WO 2003-HU41	20030611
WO 2003106456	A3	20040304		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
HU 2002002001	A2	20050829	HU 2002-2001	20020614
AU 2003244880	A1	20031231	AU 2003-244880	20030611
BR 2003011771	A	20050329	BR 2003-11771	20030611
EP 1517907	A2	20050330	EP 2003-738355	20030611
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1662530	A	20050831	CN 2003-813858	20030611
JP 2005532369	T	20051027	JP 2004-513288	20030611
NZ 537633	A	20060831	NZ 2003-537633	20030611
IN 2004KN01852	A	20051230	IN 2004-KN1852	20041206
ZA 2004009907	A	20060830	ZA 2004-9907	20041207
KR 756761	B1	20070907	KR 2004-720277	20041213
MX 2004PA12691	A	20050815	MX 2004-PA12691	20041214
NO 2005000199	A	20050304	NO 2005-199	20050113
US 2005153973	A1	20050714	US 2005-518114	20050321
PRIORITY APPLN. INFO.:			HU 2002-2001	A 20020614
			WO 2003-HU41	W 20030611
OTHER SOURCE(S):	MARPAT 140:59518			
GI				



AB Title compds. I [wherein R = (un)substituted N-containing 1- or 2-ring aromatic moieties, p-tolylsulfonyl, R1aCH₂, or R1bCO; R1a = H or (un)substituted alkyl, Ph, PhCH₂, Ph(CH₂)₂, PhCH=CH, naphthyl, pyridyl, etc.; R1b = (un)substituted alkyl, Ph, PhCH₂, Ph(CH₂)₂, PhCH=CH, naphthyl, pyridyl, etc.; B = 8-azabicyclo[3.2.1]octyl or 9-azabicyclo[3.3.1]nonyl; Z = thiazolidinediyl, (hydroxy or oxo)pyrrolidinediyl, oxazolidinediyl, or dihydropyrrolidinediyl; and salts, isomers, tautomers, hydrates, or solvates thereof] were prepared as dipeptidyl-peptidase-IV (DPP-IV) inhibitors. These compds. contain tropane building blocks. For example, substitution of tert-Bu 8-benzyl-8-azabicyclo[3.2.1]oct-3-yl-exo-carbamate with 2-chloropyrimidine gave the 8-pyrimidinyl derivative (67%), which was converted to the amine (77%) using TFA. Amidation of (4R)-3-(tert-butoxycarbonyl)thiazolidine-4-carboxylic acid (88%), followed by deprotection (81%), addition of chloroacetyl chloride (75%), and reduction of

the

amide to the nitrile (43%), gave (4R)-3-(2-chloroacetyl)thiazolidine-4-carbonitrile. Coupling of 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine with the nitrile using TEA in MeCN afforded II (53%). Compds. of the invention show low IC₅₀ values for DPP-IV enzyme inhibitory activity in comparison with known compds. and are strong, long-acting enzyme inhibitors (no data). Thus, I and their pharmaceutical compns. are useful for the treatment of DPP-IV related diseases.

IT 637018-37-2P 637018-38-3P 637018-39-4P
637018-40-7P 637018-41-8P 637018-42-9P
637018-43-0P 637018-44-1P 637018-45-2P
637018-53-2P 637018-54-3P 637018-55-4P
637018-56-5P 637018-57-6P 637018-58-7P
637018-59-8P 637018-60-1P 637018-74-7P
637018-84-9P 637019-04-6P 637019-05-7P
637330-99-5P 637331-04-5P 637331-18-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

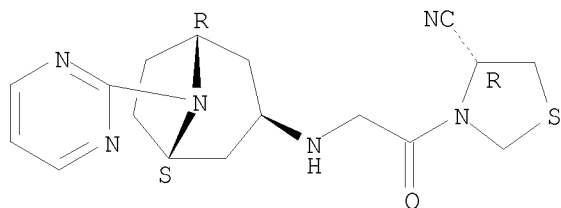
(preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as DPP-IV inhibitors)

RN 637018-37-2 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

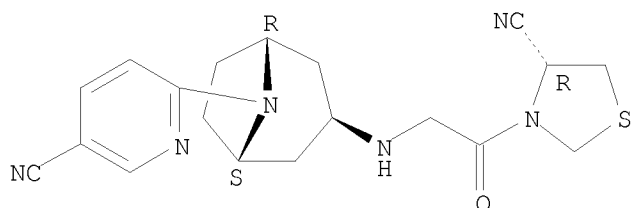
10/513699



RN 637018-38-3 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

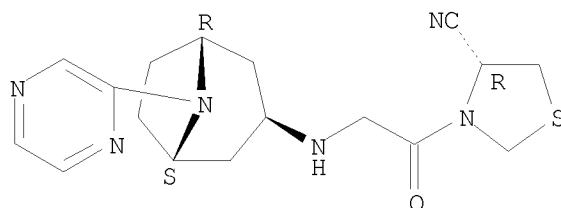


● 2 HCl

RN 637018-39-4 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



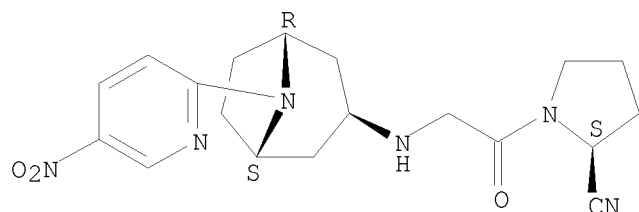
● 2 HCl

RN 637018-40-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

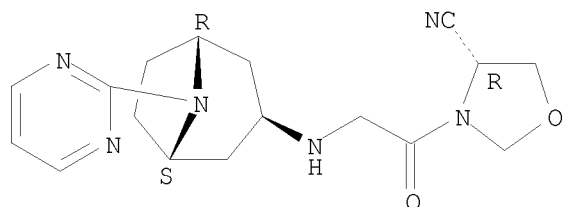
10/513699



RN 637018-41-8 CAPLUS

CN 4-Oxazolidinecarbonitrile, 3-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

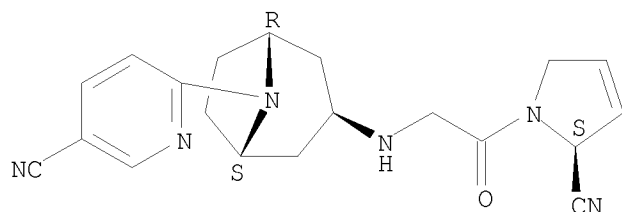
Absolute stereochemistry.



RN 637018-42-9 CAPLUS

CN 1H-Pyrrole-2-carbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-2,5-dihydro-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



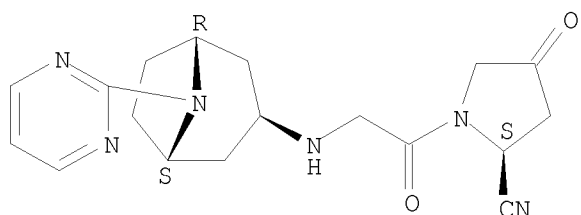
● 2 HCl

RN 637018-43-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-oxo-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

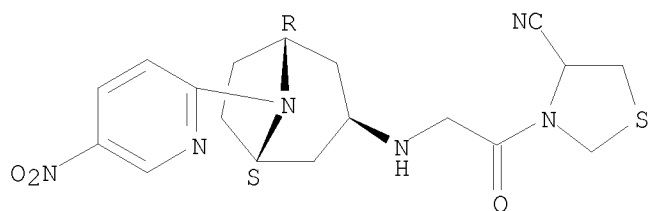
10/513699



● 2 HCl

RN 637018-44-1 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

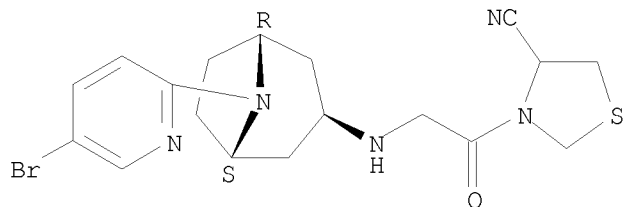
Relative stereochemistry.



● 2 HCl

RN 637018-45-2 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

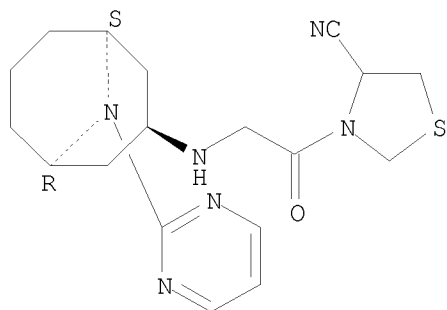
Relative stereochemistry.



RN 637018-53-2 CAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699

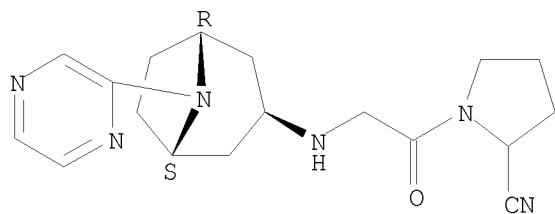


● 2 HCl

RN 637018-54-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



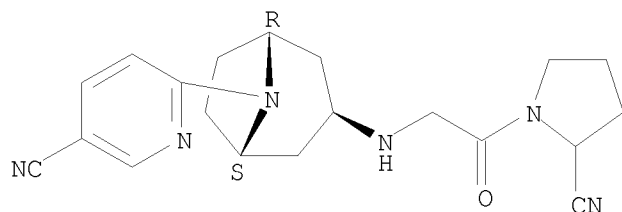
● 2 HCl

RN 637018-55-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699

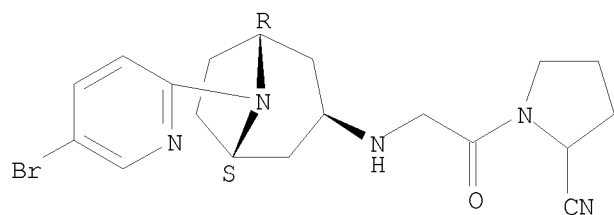


● 2 HCl

RN 637018-56-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

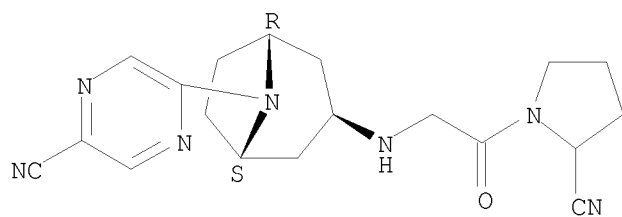
Relative stereochemistry.



RN 637018-57-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

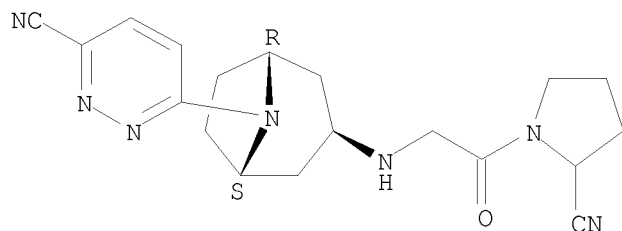


RN 637018-58-7 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.

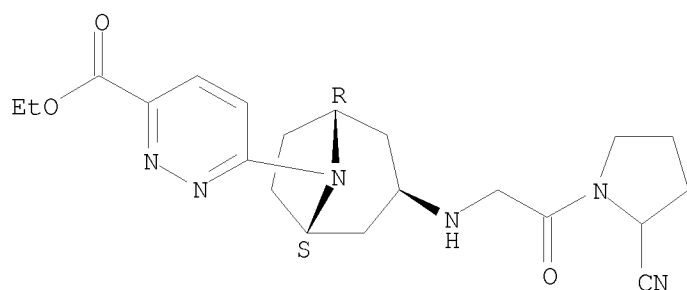
10/513699



RN 637018-59-8 CAPLUS

CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

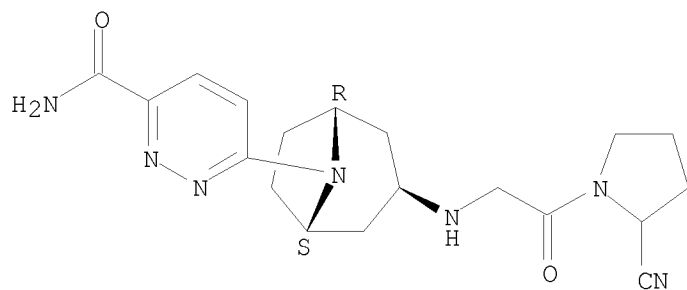


● HCl

RN 637018-60-1 CAPLUS

CN 3-Pyridazinecarboxamide, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



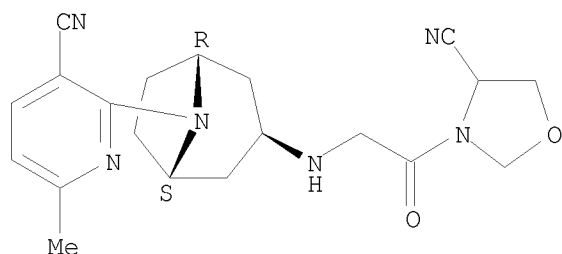
● HCl

10/513699

RN 637018-74-7 CAPLUS

CN 4-Oxazolidinecarbonitrile, 3-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

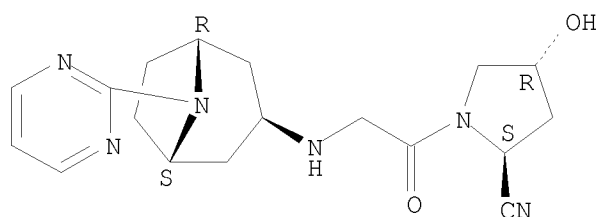


● 2 HCl

RN 637018-84-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-hydroxy-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

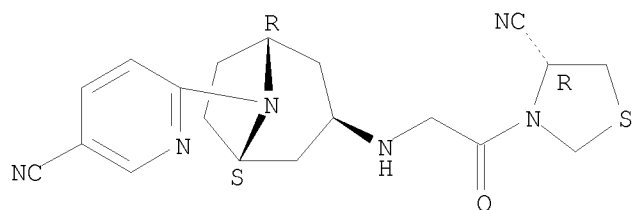
Absolute stereochemistry.



RN 637019-04-6 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

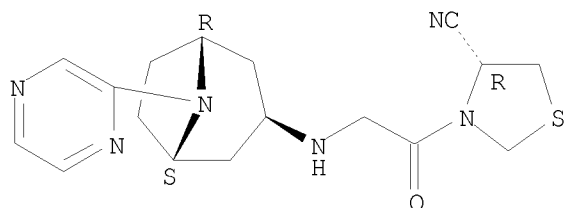


RN 637019-05-7 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

10/513699

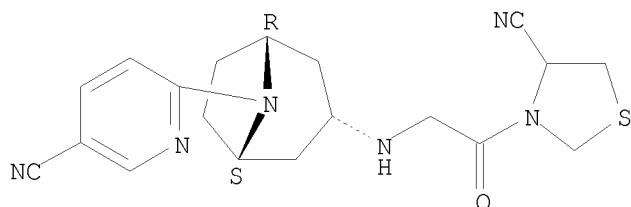
Absolute stereochemistry.



RN 637330-99-5 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

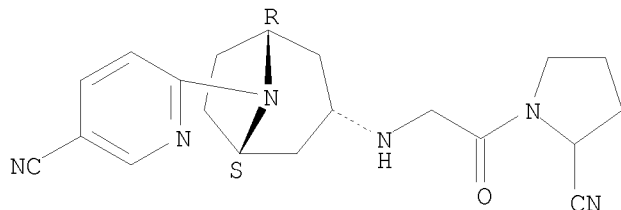
Relative stereochemistry.



RN 637331-04-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

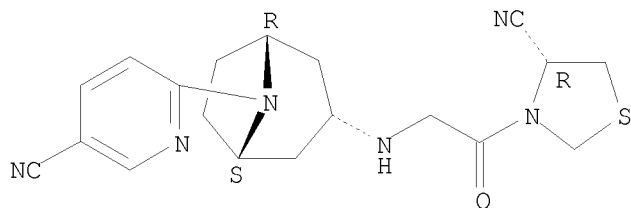
Relative stereochemistry.



RN 637331-18-1 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/513699

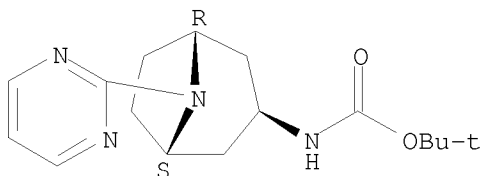
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596817-67-3P 596817-70-8P 596817-71-9P
596817-72-0P 596817-78-6P 596817-92-4P
637331-09-0P 637331-13-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or
[[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as
DPP-IV inhibitors)

RN 596816-99-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

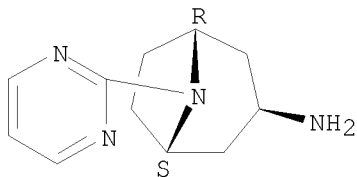
Relative stereochemistry.



RN 596817-00-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX
NAME)

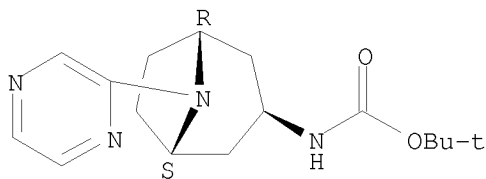
Relative stereochemistry.



RN 596817-03-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

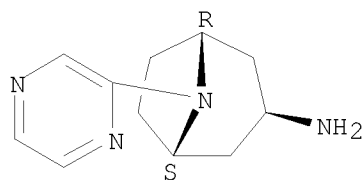


RN 596817-04-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX
NAME)

10/513699

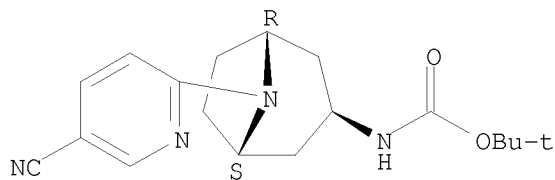
Relative stereochemistry.



RN 596817-10-6 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

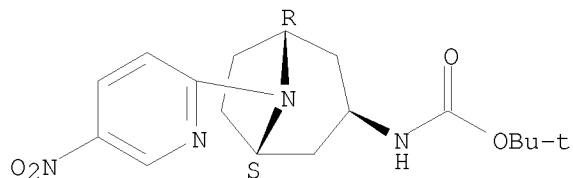
Relative stereochemistry.



RN 596817-11-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

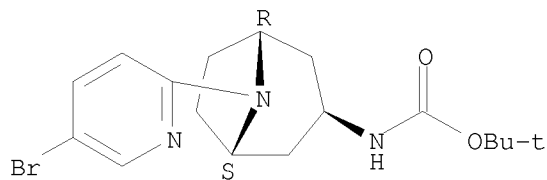
Relative stereochemistry.



RN 596817-14-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

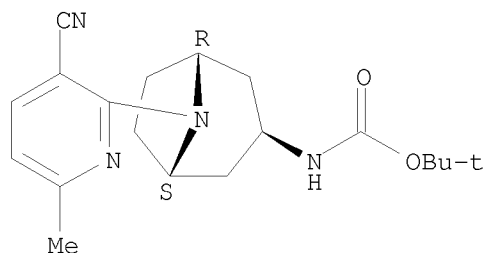


RN 596817-15-1 CAPLUS

CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/513699

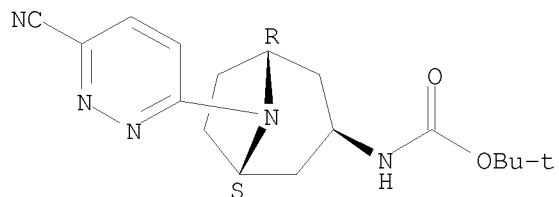
Relative stereochemistry.



RN 596817-16-2 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

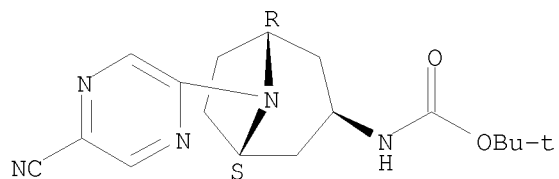
Relative stereochemistry.



RN 596817-22-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

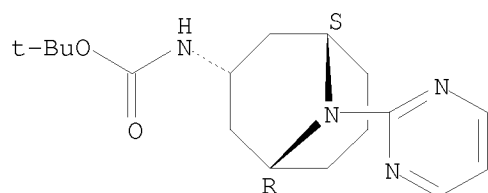
Relative stereochemistry.



RN 596817-37-7 CAPLUS

CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

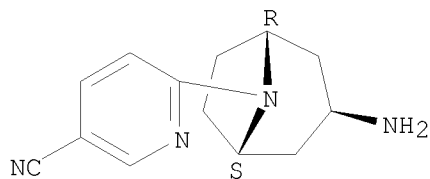
Erich Leese

10/513699

RN 596817-66-2 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(CA INDEX NAME)

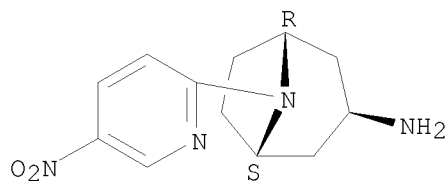
Relative stereochemistry.



RN 596817-67-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)- (CA
INDEX NAME)

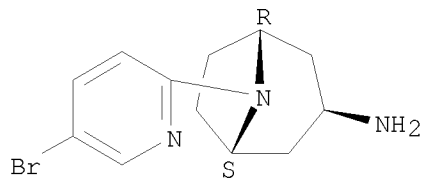
Relative stereochemistry.



RN 596817-70-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA
INDEX NAME)

Relative stereochemistry.

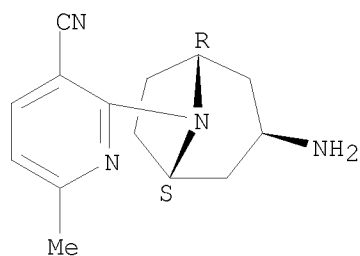


RN 596817-71-9 CAPLUS

CN 3-Pyridinecarbonitrile, 2-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-
methyl- (CA INDEX NAME)

Relative stereochemistry.

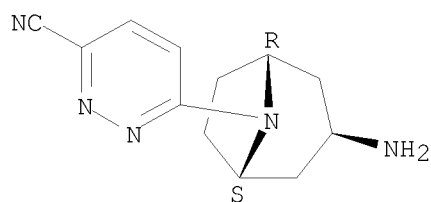
10/513699



RN 596817-72-0 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(CA INDEX NAME)

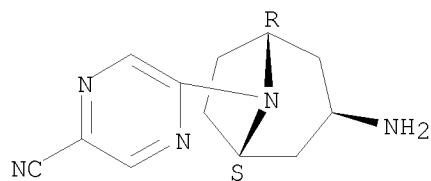
Relative stereochemistry.



RN 596817-78-6 CAPLUS

CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(9CI) (CA INDEX NAME)

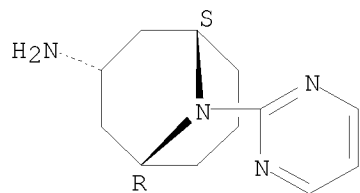
Relative stereochemistry.



RN 596817-92-4 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



RN 637331-09-0 CAPLUS

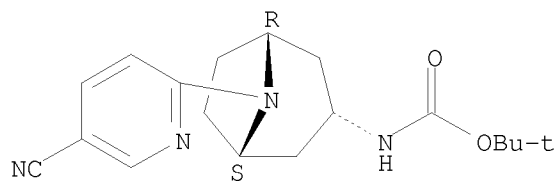
<12/04/2007>

Erich Leese

10/513699

CN Carbamic acid, [(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

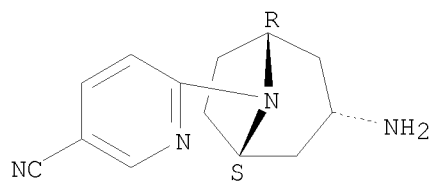
Relative stereochemistry.



RN 637331-13-6 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

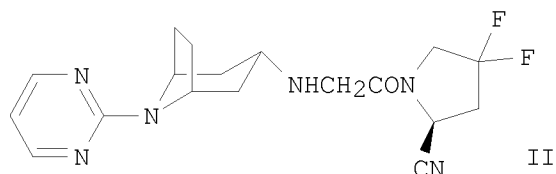
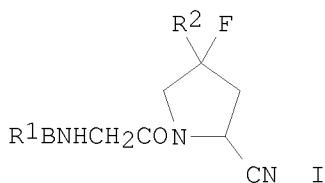
Relative stereochemistry.



10/513699

L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:719461 CAPLUS
DOCUMENT NUMBER: 139:245893
TITLE: Preparation of aminoacetylpyrrolidinecarbonitriles as
inhibitors of DPP-IV
INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori,
Sandor; Boronkay, Eva; Bovy, Philippe; Kanai, Karoly;
Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos
T.; Urban-Szabo, Katalin; Varga, Marton
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.; et al.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003074500	A2	20030912	WO 2003-HU17	20030304
WO 2003074500	A3	20031218		
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HU 2002000849	A2	20040830	HU 2002-849	20020306
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BR 2003007960	A	20050215	BR 2003-7960	20030304
CN 1639159	A	20050713	CN 2003-805263	20030304
JP 2005529078	T	20050929	JP 2003-572969	20030304
NZ 535662	A	20070531	NZ 2003-535662	20030304
CN 1990486	A	20070704	CN 2006-10164020	20030304
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PRIORITY APPLN. INFO.:			HU 2002-849	A 20020306
			CN 2003-805263	A3 20030304
			WO 2003-HU17	W 20030304
OTHER SOURCE(S):	MARPAT 139:245893			
GI				



AB Title compds. I [R1 = (un)substituted N heteroarom., thienyl, furyl, CH2Ph, tosyl, acyl; B = N heterocyclic; R2 = H, F] were prepared for use as dipeptidyl peptidase IV (DPP-IV) inhibitors with $IC_{50} \leq 100$ nM, useful in the treatment of diabetes. Thus, the title compound II was prepared from 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine and (2S)-1-chloroacetyl-4,4-difluoro-2-pyrrolidinecarbonitrile, each prepared in several steps.

IT 596816-99-8P 596817-00-4P 596817-03-7P
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 596817-11-7P 596817-12-8P 596817-13-9P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

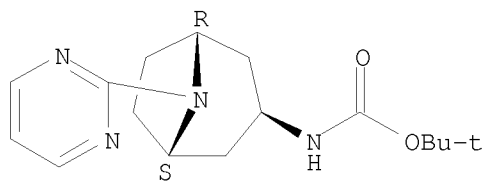
(preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV)

RN 596816-99-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

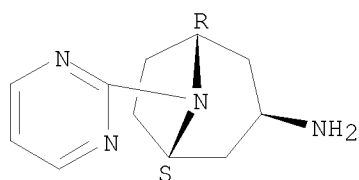
Relative stereochemistry.

10/513699



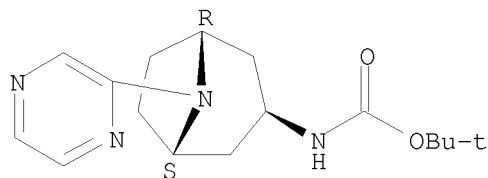
RN 596817-00-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



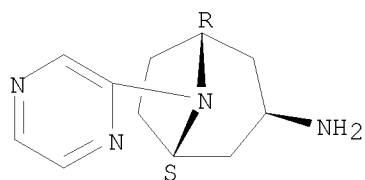
RN 596817-03-7 CAPLUS
CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596817-04-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

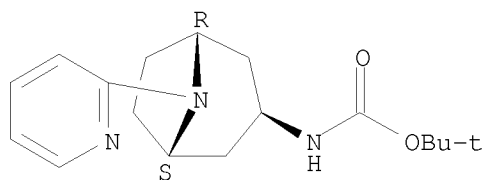
Relative stereochemistry.



RN 596817-09-3 CAPLUS
CN Carbamic acid, [(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

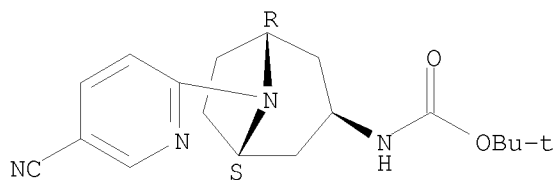
10/513699



RN 596817-10-6 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

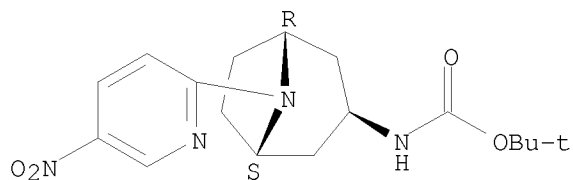
Relative stereochemistry.



RN 596817-11-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

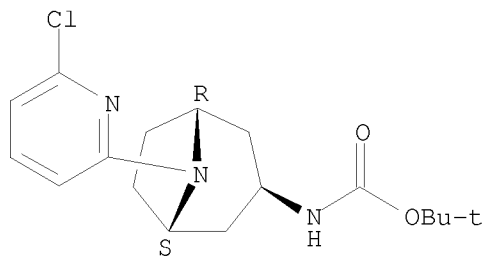
Relative stereochemistry.



RN 596817-12-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

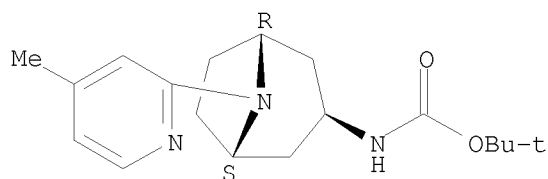


RN 596817-13-9 CAPLUS

CN Carbamic acid, [(3-exo)-8-(4-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/513699

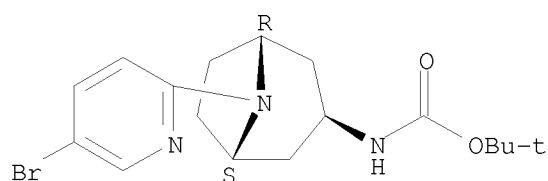
Relative stereochemistry.



RN 596817-14-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

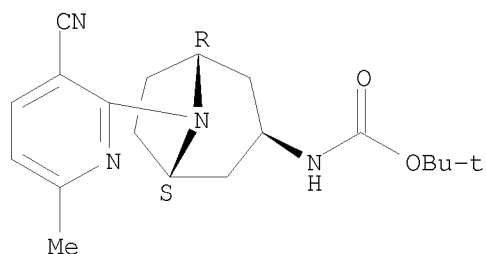
Relative stereochemistry.



RN 596817-15-1 CAPLUS

CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

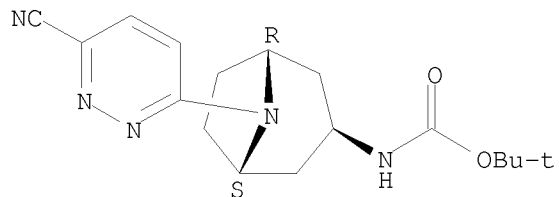
Relative stereochemistry.



RN 596817-16-2 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

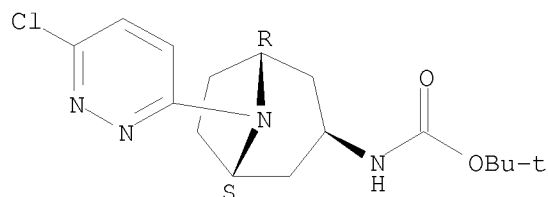


10/513699

RN 596817-17-3 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

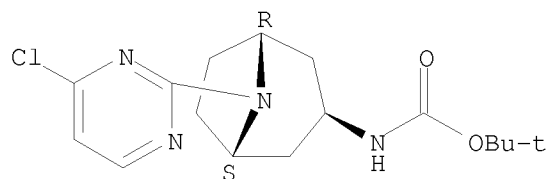
Relative stereochemistry.



RN 596817-18-4 CAPLUS

CN Carbamic acid, [(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

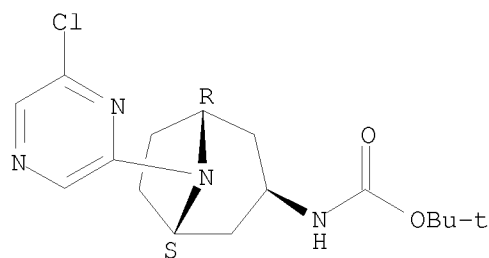
Relative stereochemistry.



RN 596817-19-5 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

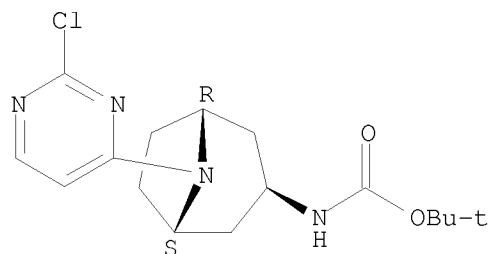


RN 596817-20-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

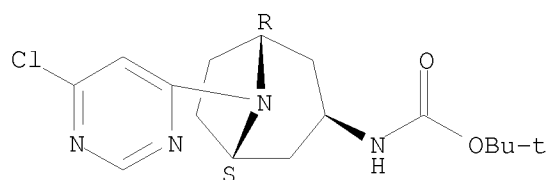
10/513699



RN 596817-21-9 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

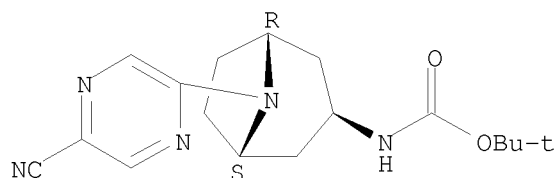
Relative stereochemistry.



RN 596817-22-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

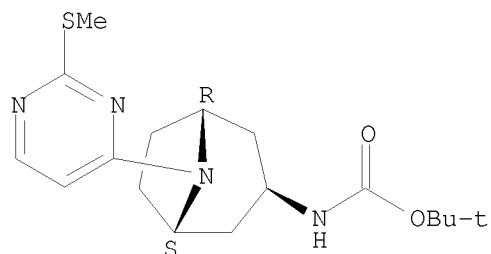
Relative stereochemistry.



RN 596817-23-1 CAPLUS

CN Carbamic acid, [(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

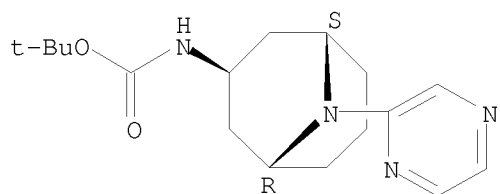
Erich Leese

10/513699

RN 596817-34-4 CAPLUS

CN Carbamic acid, [(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

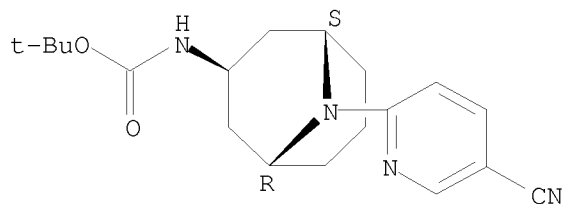
Relative stereochemistry.



RN 596817-35-5 CAPLUS

CN Carbamic acid, [(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

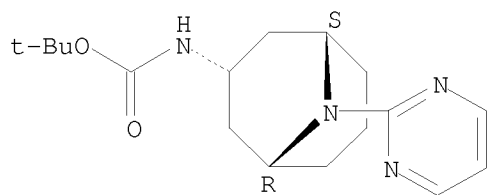
Relative stereochemistry.



RN 596817-37-7 CAPLUS

CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

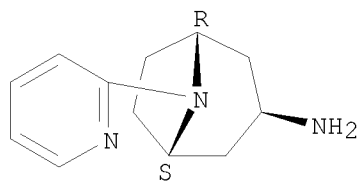


RN 596817-65-1 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.

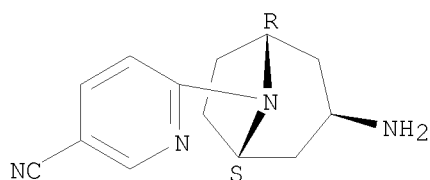
10/513699



RN 596817-66-2 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(CA INDEX NAME)

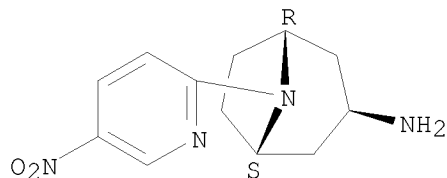
Relative stereochemistry.



RN 596817-67-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)-
(CA INDEX NAME)

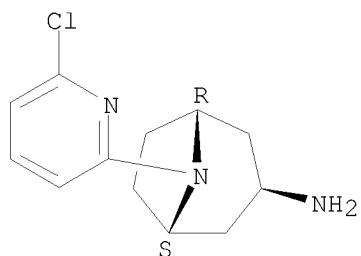
Relative stereochemistry.



RN 596817-68-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-2-pyridinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



RN 596817-69-5 CAPLUS

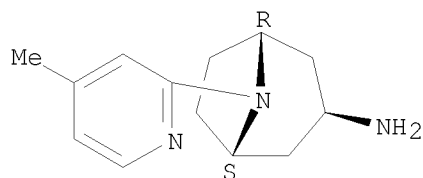
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-methyl-2-pyridinyl)-, (3-exo)-
(CA INDEX NAME)

<12/04/2007>

Erich Leese

10/513699

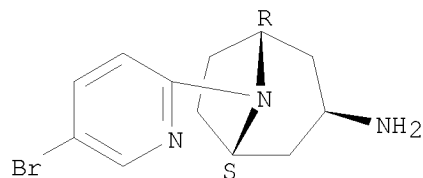
Relative stereochemistry.



RN 596817-70-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

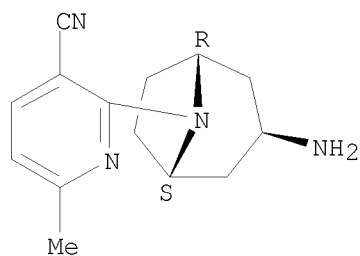
Relative stereochemistry.



RN 596817-71-9 CAPLUS

CN 3-Pyridinecarbonitrile, 2-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-methyl- (CA INDEX NAME)

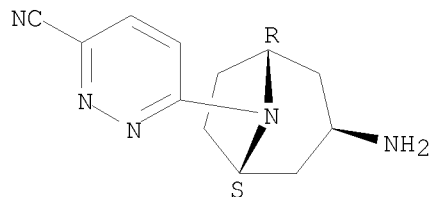
Relative stereochemistry.



RN 596817-72-0 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

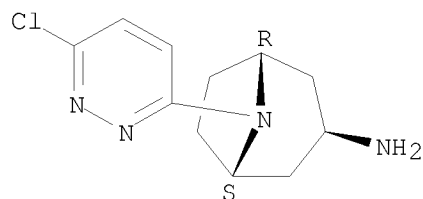
Relative stereochemistry.



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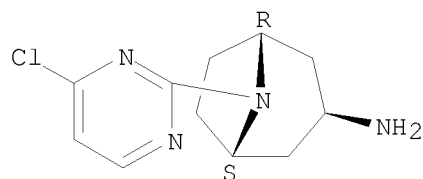
RN 596817-73-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-3-pyridazinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



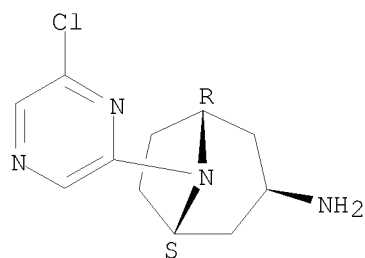
RN 596817-74-2 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-chloro-2-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.



RN 596817-75-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloropyrazinyl)-, (3-exo)- (9CI)
(CA INDEX NAME)

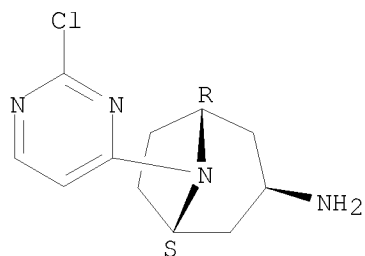
Relative stereochemistry.



RN 596817-76-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-chloro-4-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

Relative stereochemistry.

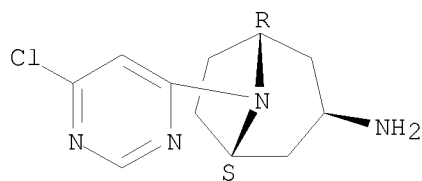
10/513699



RN 596817-77-5 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-4-pyrimidinyl)-, (3-exo)-
(CA INDEX NAME)

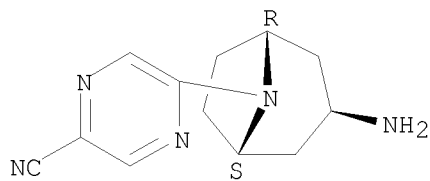
Relative stereochemistry.



RN 596817-78-6 CAPLUS

CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-
(9CI) (CA INDEX NAME)

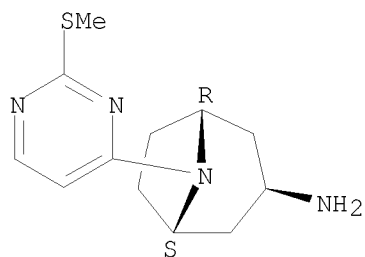
Relative stereochemistry.



RN 596817-79-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[2-(methylthio)-4-pyrimidinyl]-,
(3-exo)- (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

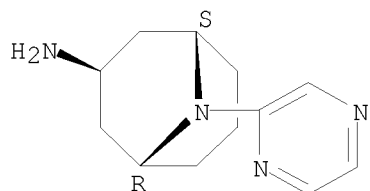
Erich Leese

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RN 596817-89-9 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

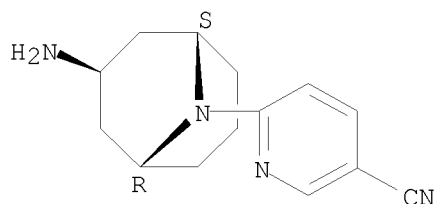
Relative stereochemistry.



RN 596817-90-2 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]- (9CI) (CA INDEX NAME)

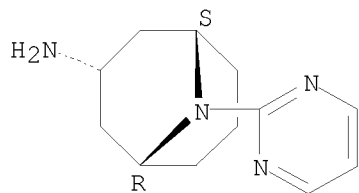
Relative stereochemistry.



RN 596817-92-4 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.

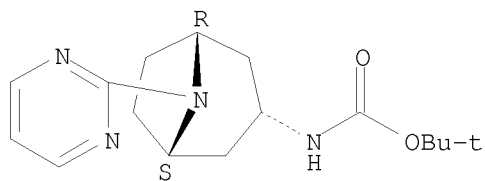


RN 599165-27-2 CAPLUS

CN Carbamic acid, [(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

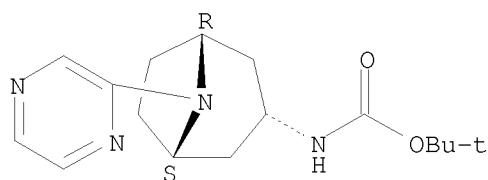
10/513699



RN 599165-28-3 CAPLUS

CN Carbamic acid, [(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

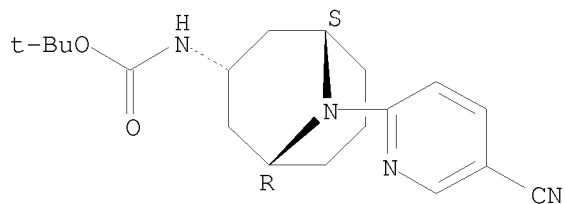
Relative stereochemistry.



RN 599165-29-4 CAPLUS

CN Carbamic acid, [(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

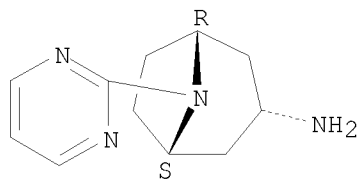
Relative stereochemistry.



RN 599165-31-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.

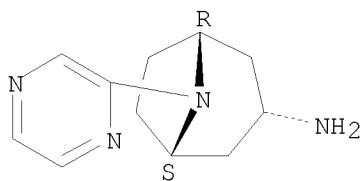


RN 599165-32-9 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

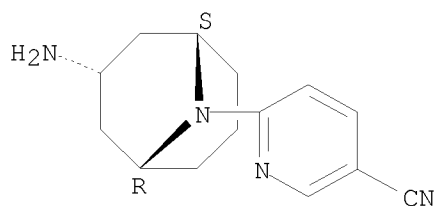
10/513699



RN 599165-33-0 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]-
(9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 596816-23-8P 596816-26-1P 596816-27-2P
596816-28-3P 596816-29-4P 596816-30-7P
596816-31-8P 596816-32-9P 596816-33-0P
596816-34-1P 596816-35-2P 596816-36-3P
596816-37-4P 596816-38-5P 596816-39-6P
596816-40-9P 596816-41-0P 596816-51-2P
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599165-36-3P

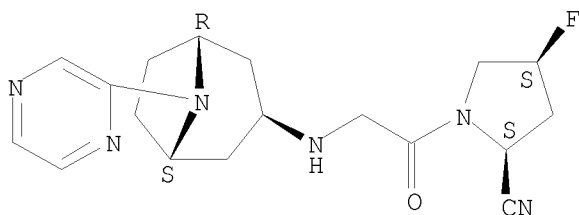
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-IV)

RN 596816-23-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



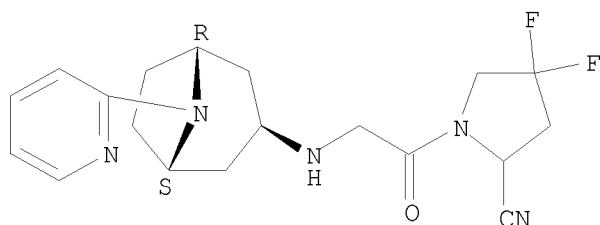
● 2 HCl

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RN 596816-26-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

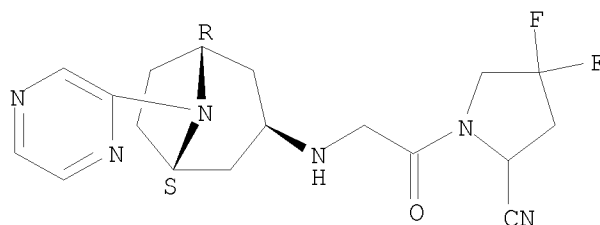


● 2 HCl

RN 596816-27-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



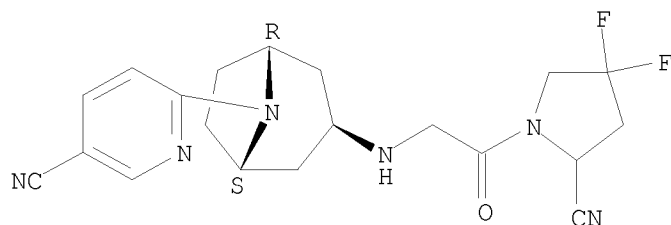
● 2 HCl

RN 596816-28-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

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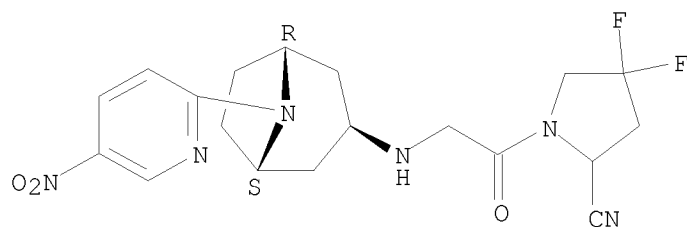


● 2 HCl

RN 596816-29-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

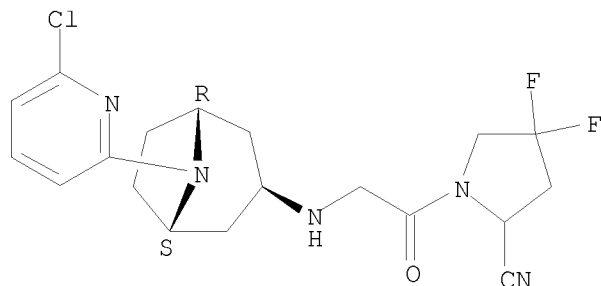
Relative stereochemistry.



RN 596816-30-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 2 HCl

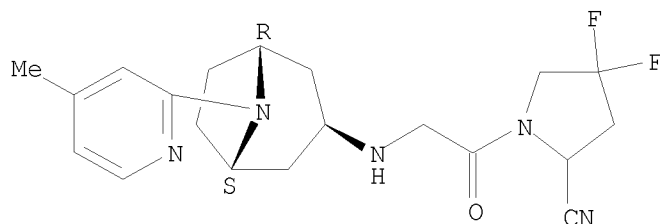
RN 596816-31-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(4-methyl-2-

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pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride
(9CI) (CA INDEX NAME)

Relative stereochemistry.

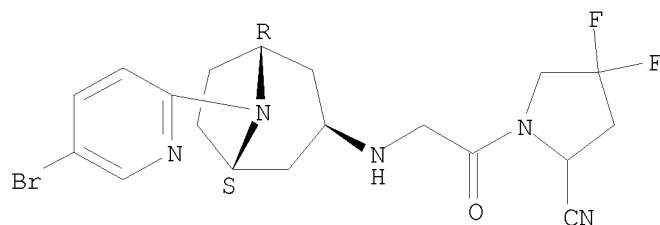


● 3 HCl

RN 596816-32-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

Relative stereochemistry.



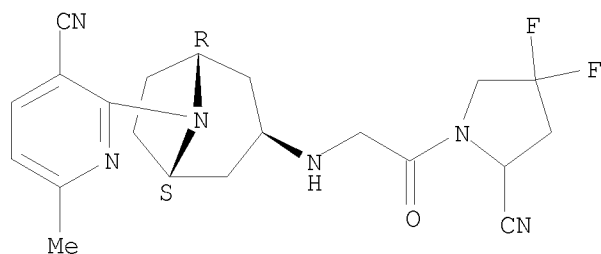
● 2 HCl

RN 596816-33-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

Relative stereochemistry.

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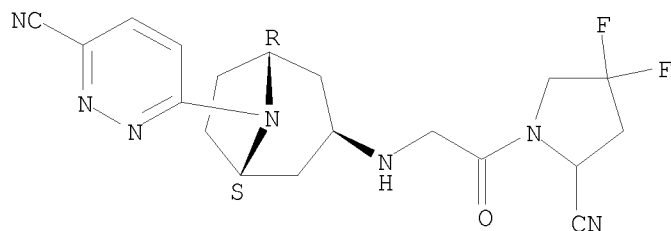


● 2 HCl

RN 596816-34-1 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[[2-(2-cyano-4,4-difluoro-1-pyrrolidiny]l)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

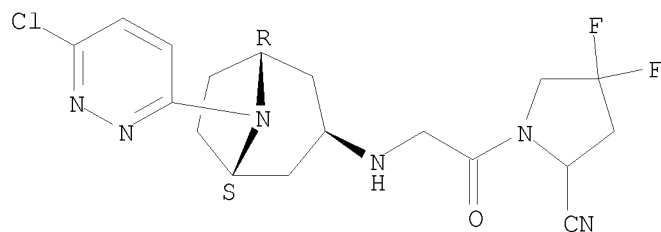
Relative stereochemistry.



RN 596816-35-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 2 HCl

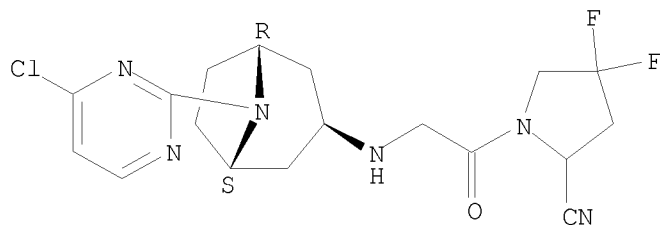
RN 596816-36-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride

10/513699

(9CI) (CA INDEX NAME)

Relative stereochemistry.

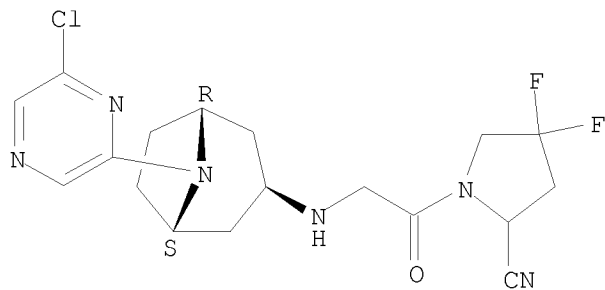


● 2 HCl

RN 596816-37-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

Relative stereochemistry.



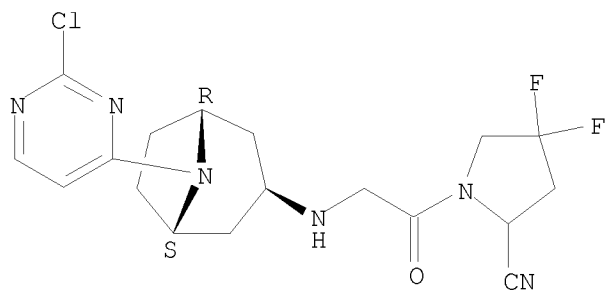
● 2 HCl

RN 596816-38-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride
(9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699

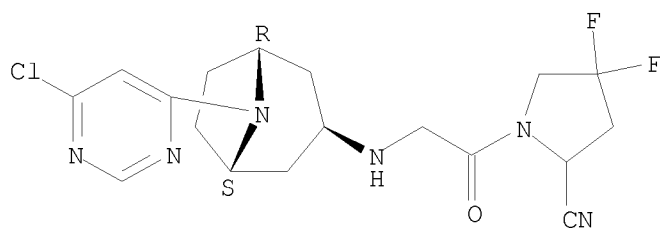


● 2 HCl

RN 596816-39-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



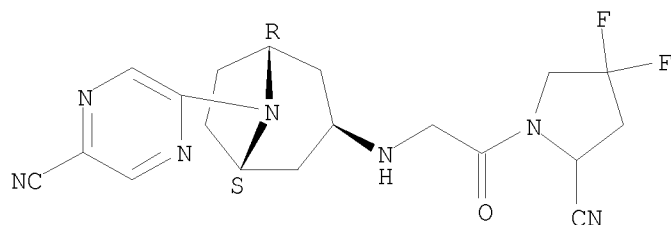
● 2 HCl

RN 596816-40-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, hydrochloride (2:3) (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699

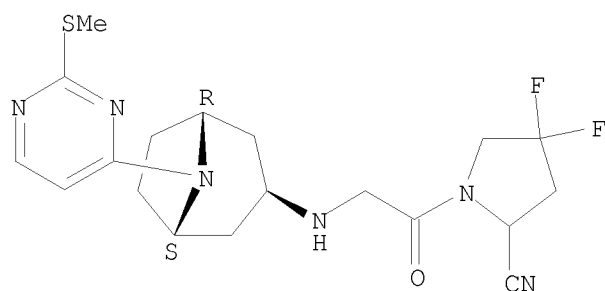


● 3/2 HCl

RN 596816-41-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

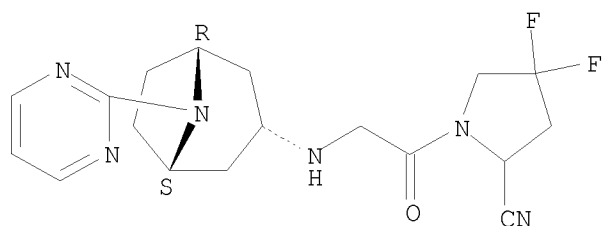


● 2 HCl

RN 596816-51-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596816-52-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

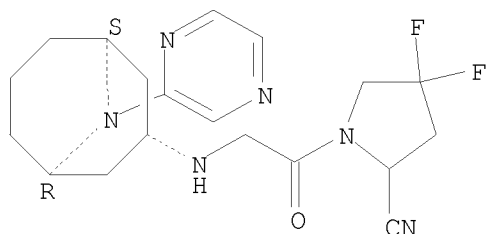
<12/04/2007>

Erich Leese

10/513699

NAME)

Relative stereochemistry.

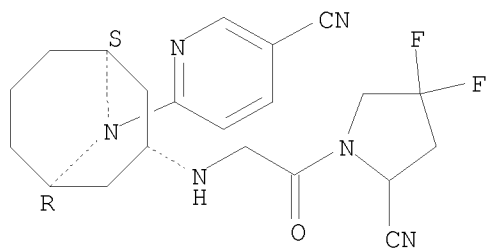


● 2 HCl

RN 596816-53-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

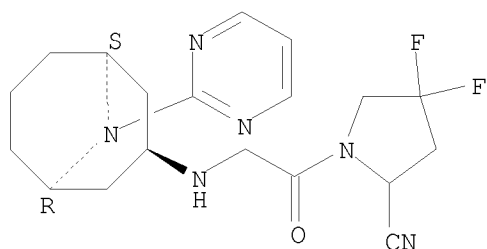


● 2 HCl

RN 596816-56-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



<12/04/2007>

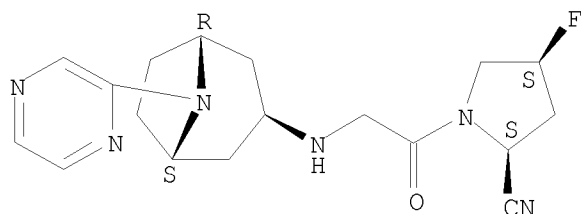
Erich Leese

10/513699

RN 596818-14-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

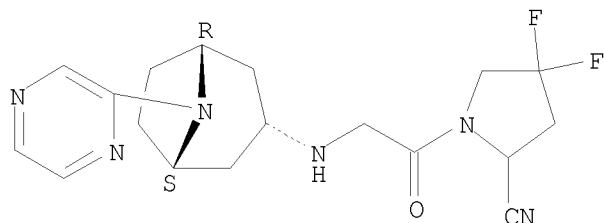
Absolute stereochemistry.



RN 599165-24-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



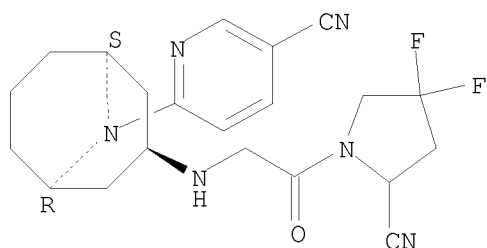
● 3 HCl

RN 599165-25-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699

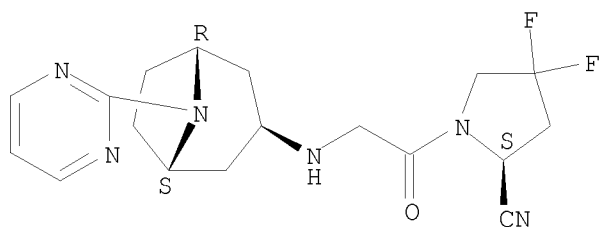


● 2 HCl

RN 599165-36-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



<12/04/2007>

Erich Leese

L3 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:964330 CAPLUS

DOCUMENT NUMBER: 138:39295

TITLE: Preparation of heterocyclic compounds as Rho-kinase inhibitors

INVENTOR(S): Imazaki, Naonori; Kitano, Masafumi; Ohashi, Naohito; Matsui, Kazuki

PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan

SOURCE: PCT Int. Appl., 425 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

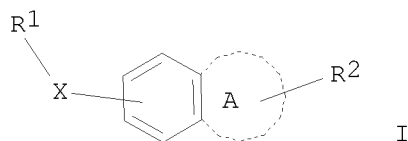
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100833	A1	20021219	WO 2002-JP5609	20020606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306284	A1	20021223	AU 2002-306284	20020606
EP 1403255	A1	20040331	EP 2002-733352	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004138286	A1	20040715	US 2003-480526	20031212
US 7199147	B2	20070403		
PRIORITY APPLN. INFO.:			JP 2001-176826	A 20010612
			JP 2001-398992	A 20011228
			WO 2002-JP5609	W 20020606

OTHER SOURCE(S): MARPAT 138:39295

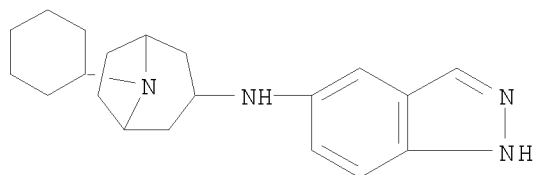
GI



AB The title compds. I [wherein one to four groups represented by the general formula R¹-X are present and may be the same or different from each other; A is a saturated or unsatd. five-membered heterocycle; X is a single bond, N(R³), O, S, or the like; R¹ is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; R² is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; and R³ is hydrogen, substituted or unsubstituted alkyl, or the like] are prepared N-(1-Benzyl-4-piperidinyl)-1H-indazole-5-amine dihydrochloride monohydrate in vitro showed IC₅₀ of 0.4 μL/mL against Rho-kinase.

10/513699

IT 478837-97-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of heterocyclic compds. as Rho-kinase inhibitors)
RN 478837-97-7 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-N-1H-indazol-5-yl- (CA
INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:827020 CAPLUS

DOCUMENT NUMBER: 136:294764

TITLE: Synthesis of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole analogues and their binding affinities for dopamine D2 and D3 receptors

AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.

CORPORATE SOURCE: Department of Radiology-PET Center, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA

SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(12), 3113-3122

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:294764

AB A series of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole derivs. was prepared and their affinity for dopamine D2 and D3 receptors was measured using in vitro binding assays. Several oxadiazole analogs were also prepared and tested for their affinity for dopamine D2 and D3 receptors. The results of receptor binding studies indicated that the incorporation of an imidazole moiety between the Ph ring and the basic nitrogen did not significantly increase the selectivity for dopamine D3 receptors, whereas the incorporation of an oxadiazole at the same region resulted in a total loss of affinity for both dopamine receptor subtype binding sites. The most selective compound in this series is 6,7-dimethoxy-2-[[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-1,2,3,4-tetrahydroisoquinoline, which has a D3 receptor affinity of 21 nM and a 7-fold selectivity for D3 vs. D2 receptors. The binding affinity for σ_1 and σ_2 receptors was also measured, and the results showed that several analogs were selective σ_1 receptor ligands.

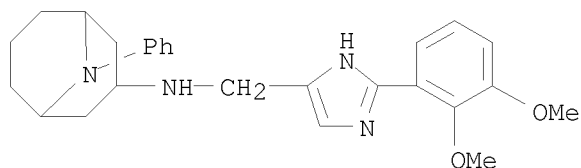
IT 407610-27-9P 407610-28-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and dopamine D2 and D3 receptor affinity of 2-(2,3-dimethoxyphenyl)-1H-imidazole-4-methanamine derivs.)

RN 407610-27-9 CAPLUS

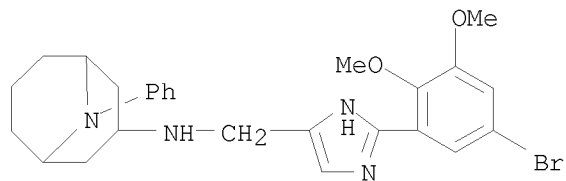
CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)



RN 407610-28-0 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[[2-(5-bromo-2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)

10/513699



REFERENCE COUNT:

28

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:229244 CAPLUS

DOCUMENT NUMBER: 135:13871

TITLE: Synthesis and structure-activity relationships of naphthamides as dopamine D3 receptor ligands

AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.

CORPORATE SOURCE: Department of Radiology-PET Center and Department of Physiology Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(11), 1815-1826

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:13871

AB A series of naphthamides were synthesized, and the affinities of these compds. were determined for dopamine D2 and D3 receptors using radioligand binding techniques. The naphthamide compds. that were prepared include N-(1-alkylpiperidin-4-yl)-4-bromo-1-methoxy-2-naphthamides (1-6), (S)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (7-12), (R)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (13-18), (S)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (19-25), (R)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (26-31), and N-(9-alkyl-9-azabicyclo[3.3.1]nonan-3 β -yl)-4-bromo-1-methoxy-2-naphthamides (32, 33). The results of in vitro radioligand binding studies indicated that the majority of the naphthamide analogs bound with high affinity at both the D2 and D3 dopamine receptor subtypes and most of the compds. demonstrated some selectivity for the dopamine D3 dopamine receptor subtype. These results demonstrated that both the structure of the central amine moiety (piperidine, pyrrolidine, and 9-azabicyclo[3.3.1]nonane) ring and the N-(alkyl) substitution on the amine significantly effects the binding affinity at D2 and D3 dopamine receptors. The bulkiness of the N-(1-alkyl) substituent was found to (a) have no effect on pharmacol. selectivity, (b) increase the affinity at D3 receptors, or (c) decrease the affinity at D2 receptors. The most potent analog in this series was (S)-N-(1-cycloheptylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamide (10), which had equilibrium dissociation (K_i) values of

1.8

and 0.2 nM for D2 and D3 receptors, resp. The most selective analog was (R)-N-(1-cycloheptyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamide (30), which had K_i values of 62.8 and 2.4 nM for D2 and D3 receptors, resp. Radioligand binding results for σ receptors indicated that the structure of the amine moiety and the N-(1-alkyl) substitutions also significantly influence the affinity and selectivity of these compds. at the σ_1 and σ_2 sigma receptor subtypes. The two naphthamides containing a 9-azabicyclo[3.3.1]nonan-3 β -yl central ring were found to be selective for σ_2 receptors.

IT 342876-79-3P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(design and SAR of naphthamides as dopamine D3 receptor ligands)

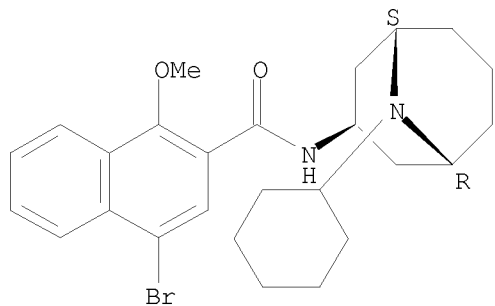
RN 342876-79-3 CAPLUS

CN 2-Naphthalenecarboxamide, 4-bromo-N-[(3-exo)-9-cyclohexyl-9-

10/513699

azabicyclo[3.3.1]non-3-yl]-1-methoxy- (CA INDEX NAME)

Relative stereochemistry.



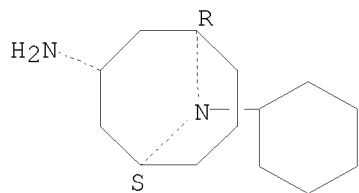
IT 342876-83-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(design and SAR of naphthamides as dopamine D3 receptor ligands)

RN 342876-83-9 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-cyclohexyl-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

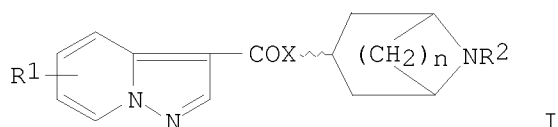
44

THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/513699

L3 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:101950 CAPLUS
DOCUMENT NUMBER: 118:101950
TITLE: Preparation of pyrazolo[1,5-a]pyridine derivatives as
serotonin 3 (5-HT3) antagonists
INVENTOR(S): Ito, Yasuo; Kato, Hideo; Yasuda, Shingo; Iwasaki,
Nobuhiko; Nishino, Hiroyuki
PATENT ASSIGNEE(S): Hokuriku Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 04257591	A	19920911	JP 1991-37776	19910208
PRIORITY APPLN. INFO.:			JP 1991-37776	19910208
OTHER SOURCE(S):	MARPAT	118:101950		
GI				



AB The title derivs. I (R1 = H, lower alkyl; R2 = H, PhCH2, lower alkyl; X = NH, O; n = 2, 3) or their pharmaceutically acceptable salts are prepared as 5-HT3 antagonists (no data). Chlorination of 1.00 g pyrazolo[1,5-a]pyridine-3-carboxylic acid in CH2Cl2 gave pyrazolo[1,5-a]pyridine-3-carbonyl chloride, which in CH2Cl2 was added dropwise into a mixture of 0.95 g exo-8-methyl-8-azabicyclo[3.3.1]octan-3-amine and Et3N in CH2Cl2 under ice cooling, then stirred at room temperature for 1.5 h to give 0.88 g exo-N-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)pyrazolo[1,5-a]pyridine-3-carboxamide.

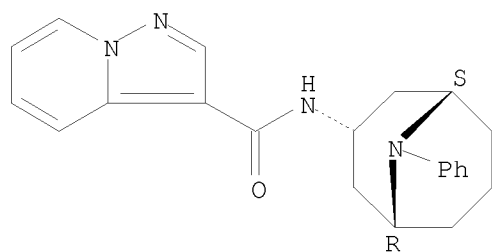
IT 145663-01-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT3 antagonist)

RN 145663-01-0 CAPLUS

CN Pyrazolo[1,5-a]pyridine-3-carboxamide, N-(9-phenyl-9-azabicyclo[3.3.1]non-3-yl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/513699



<12/04/2007>

Erich Leese

10/513699

L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1984:510862 CAPLUS

DOCUMENT NUMBER: 101:110862

ORIGINAL REFERENCE NO.: 101:16933a,16936a

TITLE: Studies on the neuroleptic benzamides. III.
Synthesis and antidopaminergic properties of new
3-nortropene derivatives

AUTHOR(S): Dostert, Philippe; Imbert, Thierry; Langlois, Michel;
Bucher, Bernard; Mocquet, Gisele

CORPORATE SOURCE: Cent. Rech., Rueil-Malmaison, 92500, Fr.

SOURCE: European Journal of Medicinal Chemistry (1984), 19(2),
105-10

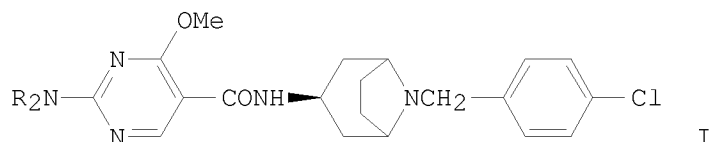
CODEN: EJMCA5; ISSN: 0009-4374

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 101:110862

GI



AB Pyrimidinecarboxamides were prepared from 4-alkoxypyrimidine-5-carboxylic acids and 3-aminonortropene derivs. and were tested for their potential antipsychotic activity. I (R = H, Me) had pharmacol. activity equivalent to that of haloperidol but had lower toxicity and lower potency to induce catalepsy. Some aspects of structure-activity relationships are discussed.

IT 76272-54-3

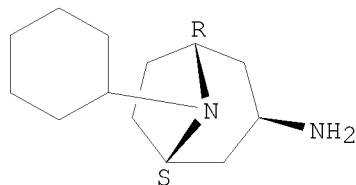
RL: RCT (Reactant); RACT (Reactant or reagent)

(acylation of, with aminomethoxypyrimidinecarboxylic acid)

RN 76272-54-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 91595-99-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn and antidopaminergic activity of)

RN 91595-99-2 CAPLUS

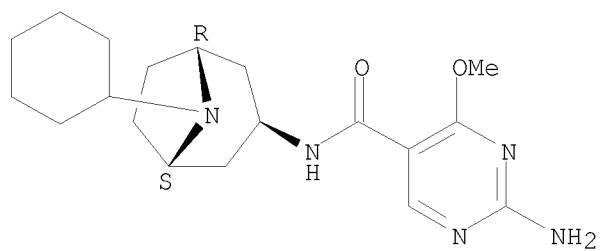
CN 5-Pyrimidinecarboxamide, 2-amino-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-4-methoxy-, exo- (9CI) (CA INDEX NAME)

<12/04/2007>

Erich Leese

10/513699

Relative stereochemistry.



<12/04/2007>

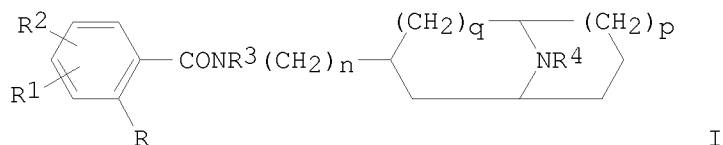
Erich Leese

10/513699

L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1981:65477 CAPLUS
DOCUMENT NUMBER: 94:65477
ORIGINAL REFERENCE NO.: 94:10669a,10672a
TITLE: Azabicycloalkyl derivatives and pharmaceutical compositions containing them
INVENTOR(S): Hadley, Michael Stewart; King, Francis David
PATENT ASSIGNEE(S): Beecham Group Ltd., UK
SOURCE: Eur. Pat. Appl., 63 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 13138	A1	19800709	EP 1979-302978	19791220
EP 13138	B1	19831207		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
EP 81054	A2	19830615	EP 1982-109116	19791220
EP 81054	A3	19830824		
EP 81054	B1	19861217		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
AT 24320	T	19870115	AT 1982-109116	19791220
EP 220339	A1	19870506	EP 1985-115575	19791220
EP 220339	B1	19891108		
R: BE, CH, DE, FR, GB, IT, NL, SE				
DK 7905539	A	19800815	DK 1979-5539	19791221
JP 55092384	A	19800712	JP 1979-170199	19791226
US 4273778	A	19810616	US 1979-107413	19791226
AU 7954255	A	19800703	AU 1979-54255	19791228
AU 527837	B2	19830324		
ES 487379	A1	19801201	ES 1979-487379	19791228
ZA 7907054	A	19801231	ZA 1979-7054	19791228
CA 1218062	A1	19870217	CA 1979-342845	19791231
US 4336259	A	19820622	US 1980-200768	19801027
US 4544660	A	19851001	US 1981-271990	19810609
US 4599420	A	19860708	US 1983-469681	19830225
CA 1220473	A2	19870414	CA 1984-446870	19840206
US 4705858	A	19871110	US 1986-824458	19860131
JP 02072178	A	19900312	JP 1989-112779	19890501
JP 03075548	B	19911202		
PRIORITY APPLN. INFO.:			GB 1978-50380	A 19781230
			GB 1979-9262	A 19790315
			GB 1979-27831	A 19790809
			EP 1979-302978	A 19791220
			EP 1982-109116	A 19791220
			US 1979-107413	A3 19791226
			CA 1979-342845	A3 19791231
			US 1981-271990	A3 19810609
			US 1983-469681	A3 19830225
OTHER SOURCE(S):	MARPAT 94:65477			
GI				



AB Azabicycloalkanes I (R = alkoxy; R1, R2 = H, halogen, CF3, acyl, acylamino, NH2, optionally substituted CONH2, SO2NH2, alkylsulfonyl, NO2; R3 = H, alkyl; R4 = optionally substituted alkyl; n, p, q = 0-2) were prepared. Thus I [R = OMe, R1 = 4-NHAc (II), R2 = 5-Cl, R3 = H, R4 = CH2Ph, n = p = 0, q = 1] was obtained as a mixture of 3' α - and 3' β -isomers by acylating 3-amino-8-benzyl-nortropine (III) and was deacylated to II (R1 = 4-NH2). III was obtained by LiAlH4 reduction of 8-benzyl-3-nortropine oxime. II (R1 = 4-NH2) inhibited apomorphine-induced stereotype behavior at ≤ 10 mg/kg s.c. in rats and was antiemetic at 0.0025 mg/kg s.c. in dogs.

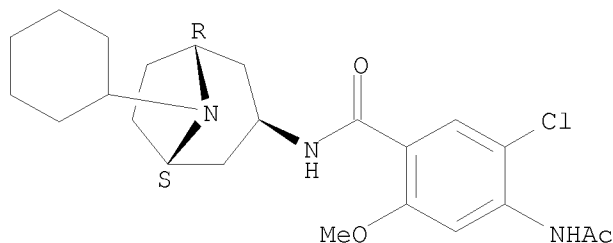
IT 76272-92-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacetylation of)

RN 76272-92-9 CAPLUS

CN Benzamide, 4-(acetyl-amino)-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 76272-91-8P

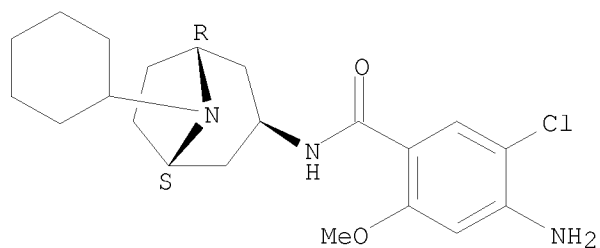
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and dopamine antagonist and antiemetic activity of)

RN 76272-91-8 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

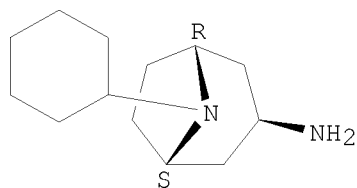
Relative stereochemistry.

10/513699



IT 76272-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, with methoxybenzoyl chloride derivative)
RN 76272-54-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX
NAME)

Relative stereochemistry.



10/513699

L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1961:82268 CAPLUS

DOCUMENT NUMBER: 55:82268

ORIGINAL REFERENCE NO.: 55:15609d-e

TITLE: State of transforming deoxyribonucleic acid (DNA)
during the first phase of bacterial transformation

AUTHOR(S): Taylor, Harriett Ephrussi

CORPORATE SOURCE: Lab. genetique physiол., Gif-sur-Yvette, Fr.

SOURCE: Comptes Rendus des Seances de la Societe de Biologie
et de Ses Filiales (1960), 154, 1951-5
CODEN: CRSBAW; ISSN: 0037-9026

DOCUMENT TYPE: Journal

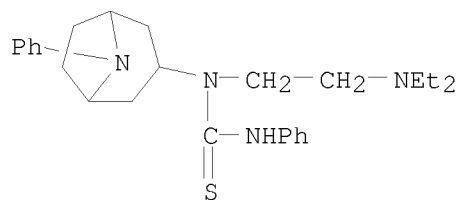
LANGUAGE: Unavailable

AB Expts. with pneumococci seemed to indicate that at the stage of fixation
of added transforming DNA the latter is firmly bound to a protein of the
receptor cell, and that it retains its high mol. weight until liberation
within the cell by growth processes.

IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-
nortropanyl)-2-thio-
RL: PREP (Preparation)
(preparation of)

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
(6CI) (CA INDEX NAME)



10/513699

L3 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1961:82267 CAPLUS

DOCUMENT NUMBER: 55:82267

ORIGINAL REFERENCE NO.: 55:15609c-d

TITLE: Action of lysozyme on Haemophilus pertussis

AUTHOR(S): Dumazert, C.; Ghiglione, C.

SOURCE: Bulletin de la Societe de Pharmacie de Marseille

(1960), 9, 145-59,161-71

CODEN: BSPMAC; ISSN: 0560-5237

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Action of lysozyme on bacterial suspensions of H. pertussis resulted in the isolation of a glucoside fraction and a protein fraction. The glucoside contains glucose, galactose, and an unidentified N base. The protein has not been fully characterized. Immunological studies on the glucoside fraction indicate properties similar to a hapten isolated from Pneumococcus.

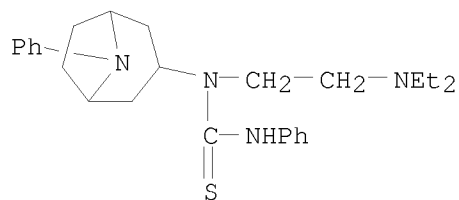
IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-

RL: PREP (Preparation)

(preparation of)

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-(6CI) (CA INDEX NAME)



L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1959:2191 CAPLUS
 DOCUMENT NUMBER: 53:2191
 ORIGINAL REFERENCE NO.: 53:430h-i, 431a-i, 432a-i
 TITLE: Tertiary amino substituted 1,5-iminocycloalkanes
 INVENTOR(S): Archer, Sydney
 PATENT ASSIGNEE(S): Sterling Drug Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2845427		19580729	US 1955-483808	19550124

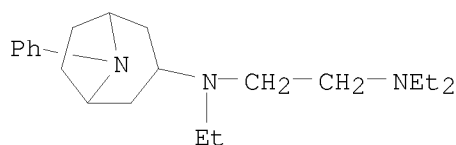
AB N-Substituted 1,5-iminocycloalkanes (I) attached at the 3-position through an O, S, or N atom to a tertiary amino alkyl group, which are useful for the reduction of hypertension (the salts and quaternary derivs. are even more active), are prepared by treating a 3-oxo derivative of I with a tertiary amino alkylamine and reducing the resulting imine by condensing the 3-alkali metal sulfide or oxide derivative of I with a tertiary amino alkyl halide and (or) by condensing 3-halo derivative of I with the alkali metal salt of a tertiary amino alkyl mercaptan or hydroxide. 3-Tropolone (30 g.), 24 g. Et₂N(CH₂)₂NH₂, 1.2 g. PtO₂, and 50 ml. EtOH was shaken 1 hr. under 50 lb. H, filtered, and the filtrate distilled to give 33.2 g. 3-(2-diethylaminoethylamino)-tropene (II), b_{0.5} 111-15°; tri-HCl salt, m. 267-71°; picrate, m. 163.5-6°; dimethiodide, m. 269°; dimethobromide, m. 289-90°. II (59 g.) was cooled to solid CO₂ temperature, 54 ml. 100% HCO₂H and 24.6 ml. 36% H₂CO added, the mixture heated on the steam bath 16 hrs., cooled and made basic, extracted with Et₂O, and the product distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropene, b_{0.8-1} 120-3°, n_{25D} 1.4871; tri-HBr salt, m. above 140°; dimethiodide, m. 242-4°; dimethobromide, m. 245-7°; diethiodide, m. 237-8°. Similarly the following 3-substituted derivs. of tropene were prepared (side chain, b.p./mm., and salts with their m.p. given): Me₂N(CH₂)₂NH, 101.5-3°/0.5 (n_{25D} 1.4880); Me₂N(CH₂)₂NMe, 104-7°/1.2 (n_{25D} 1.4900-9), di-MeI 238-41°; C₅H₁₀N(CH₂)₃NH, 141-50°/0.5; C₅H₁₀N(CH₂)₃NMe, 141-8°/0.2 (n_{25D} 1.5057), di-MeI 222-3°, tri-MeI 207-14°; C₅H₁₀N(CH₂)₂NH, 132-3°/0.5, tri-HCl 275-7°, di-MeI 293°; C₅H₁₀N(CH₂)₂NMe, 118.5-26°/0.07, tri-HBr 220-4.5°, di-MeI 259-66°, di-EtI 215-19°; C₄H₄N(CH₂)₃NH, 140-4°/0.05; C₄H₄N(CH₂)₃NMe, 129-31°/0.2 (n_{25D} 1.5031-40), di-MeI 226-8°; C₄H₄N(CH₂)₂NH, 130-5°/0.5, di-MeI 290-3°; C₄H₄N(CH₂)₂NMe, 122-4°/0.3 (n_{25D} 1.5055-60), di-MeI 205-20°; C₄H₄N(CH₂)₄NH, 142-8°/0.3 (n_{25D} 1.5038-41); C₄H₄N(CH₂)₄NMe, 138-41°/0.2 (n_{25D} 1.5029); OC₄H₈N(CH₂)₂NH, 133-5°/0.4 (n_{25D} 1.5066), tri-HCl 245-9.5°, di-MeI 264-5°; OC₄H₈N(CH₂)₂NMe, 124-30°/0.1 (n_{25D} 1.5079-83), tri-HBr 252-4°, di-MeI 218-20°; Me₂N(CH₂)₃NH, 112-14°/1.7 (n_{25D} 1.4990), picrate 230°; Me₂N(CH₂)₃NMe, 106-12°/0.5 (n_{25D} 1.4885-8), picrate 231°; Et₂N(CH₂)₃NH, 120-5°/0.1 (n_{25D} 1.4862); Et₂N(CH₂)₃NMe, 120-30°/0.1 (n_{25D} 1.4870), di-MeI 222-7°; PhMeN(CH₂)₂NH (III), 167-73°/0.1; PhEtN(CH₂)₂NH (IV), 174-7°/0.6, MeI 226-8°; p-MeC₆H₄NMe(CH₂)₂NH, 164-73°/0.3 (n_{23.5D} 1.5532);

p-MeOC₆H₄NMe(CH₂)₂NH, 179-83°/0.5 (n₂₄D 1.5560); NH(CH₂)₂NH (bis compound), 178-81°/0.6; and NMe(CH₂)₂NMe (bis compound), 192-200°/1.5, di-MeI 273-4°. II (3.8 g.) and 2.2 g. PhNCS heated in MeOH gave 3.7 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea (V), m. 170.5-2°. The following derivs. of II were prepared (group replacing the H of the secondary amine, b.p./mm., or m.p., and certain salts with their m.p. given): MeCH:CHNHCS, 97-100°; EtNHCS, 122-4°; 4-EtOC₆H₄NHCS, 160-1°; Ac (VI), 142-4°/0.09 (n₂₅D 1.4980), picrate 198-200°; EtCO (VII), 160°/0.5 (n₂₅D 1.4940-5), picrate 173-6°; and PrCO (VIII), 162-6°/0.7 (n₂₈D 1.4935), picrate 194-6°. VI, VII, and VIII were reduced with LiAlH₄ in Et₂O to the following N-substituted derivs. of II (substituent, b.p./mm., n₂₈D, and salts given): Et, 142°/2, 1.4845, di-MeI 230-1°, di-EtI 226°; Pr, 119-26°/0.1, 1.4835, picrate 223°, di-MeI 203-9°; and Bu, 125-30°/0.1, 1.4839, picrate 208-10°. Other 3-substituted tropane derivs. that were prepared are (side chain, b.p. m/m., and salts given): C₄H₄N(CH₂)₂N(CHO), 166-72°/0.9 (n₂₄D 1.5131); PhEtN(CH₂)₂N(CHO), 200-7°/0.1-0.2; PhEtN(CH₂)₂NMe, 182-7°/15 (n₂₄D 1.5518), di MeI 240-2°; p-MeC₆H₄NMe(CH₂)₂N(CHO), 95-7°; p-MeC₆H₄NMe(CH₂)₂NMe, 174-6°/0.5 (n₂₄D 1.5508-10), HCl 168°, tri-MeI 215°; p-MeOC₆H₄NMe(CH₂)₂N(CHO), 112-14°; p-MeOC₆H₄NMe(CH₂)₂NMe (IX), 162-6°/0.1 (n₂₅D 1.5518), picrate 205-7°, di-MeI 195-8°. Formic acid (26.5 ml.), 500 ml. H₂O, and 29 g. III followed by 10 ml. 37% H₂CO was heated 15 hrs. on the steam bath to give 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine (X), b_{0.6} 155-65°; di-MeI salt (XI), m. 264-7°; di-EtI salt, m. 208-10°. X was methylated in the 7-position with H₂CO and HCO₂H, b_{0.2} 163°; picrate, m. 230-1°; methiodide, m. 274-6°. XI subjected to a Hofmann degradation gave 1-[(2-dimethylaminobenzyl)vinylamino]-3-dimethylamino-5-cycloheptene; dipicrate, m. 193-4°. IV, H₂CO, and HCO₂H gave the 1-Et homolog of X, b_{0.5} 174-8° (di-MeI salt, m. 269-71°; MeI salt, m. 235-8°; di-MeBr salt, m. 262-2.5°; di-EtBr salt, m. 253-4°), and IX under these conditions gave the 7-methoxy derivative of X, b_{0.1} 180-5°; picrate, m. 239-40°. III heated with 98% HCO₂H gave 3-[2-(phenylmethyldiaminoethyl)formylamino]tropane, b_{0.5} 216-22°, which was reduced with LiAlH₄ to the N-Me derivative, b_{0.6} 160-5°; dimethiodide, m. 255°; dimethobromide, m. 258°. Tropine (60 g.) in 50 ml. MePh was added to 9.2 g. Na in 100 ml. MePh, the mixture refluxed 4 hrs. and 42.8 g. Me₂N(CH₂)₂Cl added, the mixture refluxed 3 hrs., aqueous MeOH added, and distilled to give 17.3 g. 3-(2-dimethylaminoethoxy)tropane, b_{0.9} 85-5.5°, n₂₅D 1.4836; diperchlorate, m. 243-6°; dimethiodide, m. 314-15°; diethiodide, m. 269-75°. Similarly, the following 3-substituted tropanes were prepared (side chain, b.p./mm., and salts and their m.p. given): Et₂N(CH₂)₂CO, 101°/0.07 (n₂₅D 1.4758), di-MeI 301-2°; C₅H₁₀N(CH₂)₂CO, 106-9°/0.07, di-MeI 305°; C₅H₁₀N(CH₂)₂CO, 115°/0.1, di-MeI above 305°; C₄H₄N(CH₂)₂CO, 134°/2.8 (n₂₅D 1.4932), di-MeI 313-14°; Et₂N(CH₂)₂CO(CH₂)₂CO, 94-6°/0.2, di-MeI 300°. Pseudotropine, Na, and Et₂(CH₂)₂Cl in C₆H₆ gave 3-(2-diethylaminoethoxy)pseudotropine, b_{0.25} 109-12°, n₂₅D 1.4775; dimethiodide, m. 307-8°. Tropanone (69.5 g.), 63.8 g. Et₂N(CH₂)₂NH₂, and 500 mg. ZnCl₂ in MePh was heated 64 hrs. using an H₂O separator to yield 92.2 g. 3-(2-diethylaminoethylimino)tropane (XII), b_{0.6} 117-31°. XII was reduced by Na and EtOH to a mixture of 3-(2-diethylaminoethylamino)tropane and pseudotropine. The mixture of

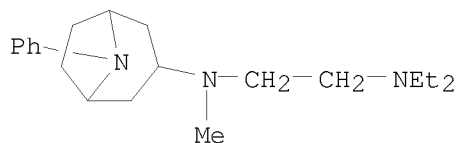
isomers and PhNCS gave V and the isomeric pseudotropine, m. 138-9.5°. By this procedure pseudopelletierine (XIII) and C₅H₁₀N(CH₂)₂NH₂ yielded 3-[2-(1-piperidyl)ethylimino]-9-methylgranatanine, b₁ 164-76°, n_{25D} 1.5235, which was reduced by Na in Me₂CH(CH₂)₃OH to a mixture of isomers of the corresponding amine which was treated with PhNCS in MeOH to yield a mixture of isomers of the thiourea (XIV), m. 174.5-6°, (XV) m. 173-4.5° (AcOEt). XIV (7.3 g.), MeOH, and 25 ml. 4N HCl in EtOH was evaporated, the residue heated 30 min. at 100°, dissolved in EtOH, and the solution cooled to yield 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine; tri-HCl salt (XVI), m. 285-7°. XV treated in this manner gave an isomer of XVI, m. 276°. Similarly, XIII with the appropriate amine gave the following 3-substituted derivs. of 9-methylgranatanine (side chain, b.p./mm., and salts with their m.p. given; when isomers were obtained, both m.p.'s given): C₄H₄N(CH₂)₂NH, 144-6°/1 (n_{24D} 1.5252); C₄H₄N(CH₂)₂NH, 155-7°/2 (n_{25D} 1.5102), di-MeI 278°; C₄H₄N(CH₂)₂(PhNHCS)N, 173-4°; Et₂N(CH₂)₂NH, 131-9°/0.7 (n_{25D} 1.5050); Et₂N(CH₂)₂NH, 128-30°/0.6 (n_{25D} 1.4920), tri-HCl 278° and 185°, di-MeI 277-9°; Et₂N(CH₂)₂(PhNHCS)N, 189-91° and 135-6°. Concentrated HCl (0.13 ml.) was added to 160 g. 2,5-diethoxytetrahydrofuran in 150 ml. H₂O, the suspension stirred 2 hrs. at 48-50° and cooled, 202 g. (EtO₂CCH₂)₂CO, 100 ml. H₂O, 107 g. PhCH₂NH₂, and 83 ml. HCl added, the mixture stirred overnight, 250 ml. HCl added, heated while 270 ml. H₂O was distilled, the residue filtered, the filtrate made basic with NaOH, 500 g. K₂CO₃ added, and the mixture extracted with Et₂O to yield 102 g. 8-benzyltropone (XVII), b_{0.4} 134-7°, n_{25D} 1.5526. XVII yielded 3-(2-diethylaminoethylamino)-8-benzyltropone, b_{0.25} 161-8°, n_{25D} 1.5235; tri-HCl salt, m. 264-6°; dimethiodide, m. 255-7°; phenylthiourea derivative, m. 138-9°. The following 8-benzyltropone derivs. are described (side chain and phenyl substituents, b.p./mm. or m.p., and salts given): 4'-MeO, 3-oxo, 179-84°/0.1 (n_{25D} 1.5538), HCl 203-4°; 4'-MeO, 3-Et₂N(CH₂)₂NH, tri-HCl 277-8°, di-MeI 229-30°; 2',3'-di-MeO, 3-oxo, 178-99°/0.5, HCl 201-2°; 2'-3'-di-MeO, 3-Et₂N(CH₂)₂NH, tri-HCl 234-7°, di-MeI 226-8°; 3',4'-OCH₂O, 3-oxo, tri-HCl 223-3.5°; 3',4'-OCH₂O, 3-Et₂N(CH₂)₂NH, tri-HCl 275-6°, di-MeI 234-7°; 3',4'-OCH₂O 3-Et₂N(CH₂)₂(PhNHCS)N, 148-9°; 4'-Cl, 3-oxo, 168-80°/0.8; 4'-Cl, 3-Et₂N(CH₂)₂NH, di-MeI 232-4°, di-MeBr 228-30.5°; 2'-Cl, 3-Et₂N(CH₂)₂(PhNHCS)N, 124-6°; 2'-Cl, 3-C₄H₄N(CH₂)₂NH, tri-HCl 253°, di-MeI 218-20°; 2'-MeO, 3-oxo, 174-81°/0.2-0.5 (n_{25D} 1.5061-5), HCl 177-8°; 2'-MeO, 3-Et₂N(CH₂)₂NH, tri-HCl 248-51°, di-MeI 218.5-21.5°; 2',4'-di-Cl, 3-oxo, 185-7°/1.5, tri-HCl 216°; and 2,4-di-Cl, 3-Et₂N(CH₂)₂NH, di-MeI 237-9°. 8-Phenyltropone, m. 107-9°, was prepared by the method used for XIII and reaction with Et₂N(CH₂)₂NH₂, PtO₂, and H gave 3-(2-diethylaminoethylamino)-8-phenyltropone (XVIII), b_{0.2} 153-68°, which with PhNCS gave the thiourea derivative, m. 161-3°, and with Ac₂O yielded N-Ac derivative of XVIII, b_{0.2} 183-98°, n_{25D} 1.5470, which was reduced to the N-Et derivative of XVIII, b_{0.9} 180-4°, n_{30D} 1.5370. PhEtN(CH₂)₂NH₂ (35 g.), 32 g. XIII, 1 g. ZnCl₂, and 200 ml. MePh gave 3-(2-phenylmethylaminoethylamino)-9-methylgranatanine, b_{0.2-0.9} 160-84°, n_{30D} 1.5575, from which the following N-substituted derivs. were prepared (b.p./mm. and salts with their m.p. given): HCO, 190-220°/0.7; Me, 161-6°/0.15, picrate 191-4°, di-MeI 225-7°; Ac, 200-14°/0.2; and Et, 162-7°/0.1, picrate 203-5°.

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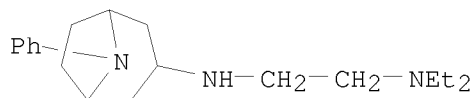
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RL: PREP (Preparation)
(preparation of)
RN 102457-13-6 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- (6CI) (CA INDEX NAME)



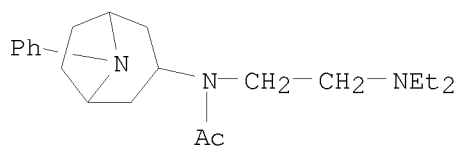
RN 102463-23-0 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 102709-02-4 CAPLUS
CN Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- (6CI) (CA INDEX NAME)



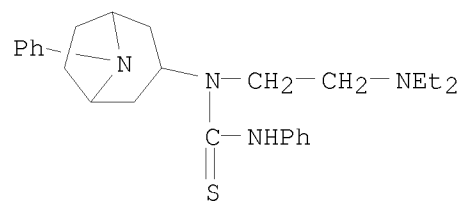
RN 110147-72-3 CAPLUS
CN Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- (6CI) (CA INDEX NAME)



RN 123935-68-2 CAPLUS

10/513699

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
(6CI) (CA INDEX NAME)



<12/04/2007>

Erich Leese

L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

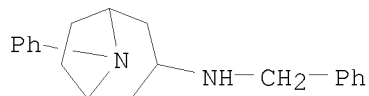
ACCESSION NUMBER: 1958:6906 CAPLUS
 DOCUMENT NUMBER: 52:6906
 ORIGINAL REFERENCE NO.: 52:1292a-i,1293a-b
 TITLE: 3-(Monocarbocyclic aryl-lower alkyl)amino-1,5-
 iminocycloalkanes
 INVENTOR(S): Archer, Sydney
 PATENT ASSIGNEE(S): Sterling Drug Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2798874		19570709	US 1955-502745	19550420

GI For diagram(s), see printed CA Issue.
 AB Compds. of the general formula $RN.CH.CH_2.(CH_2)_m.CH.CH_2.CH(NR'C_nH_{2n}Ar).CH_2$ and their salts, where R is lower alkyl, monocarbocyclic aryl, or aryl lower alkyl, R' is H or lower alkyl, m is 1-2, n is 1-6, and Ar is a monocarbocyclic aryl group, are useful in reducing hypertension and exhibit ganglionic blocking action in cats and dogs. They are prepared by reaction of a 3-tropinone (via the Robinson synthesis) and $ArC_nH_{2n}NH_2$ under hydrogenation conditions. E.g., 45 g. 3-tropinone (I), 32 g. $PhCH_2NH_2$, 1.0 g. PtO_2 , and 150 ml. EtOH are shaken 4 hrs. at 55° with H at 50 lb. per sq. in. One mole H is taken up. After filtration, the mixture is distilled and redistd. to obtain 34.8 g. 3-benzylaminotropane (II), b0.8 140-2°, n25D 1.5450; picrate, m. 160-1°. II (29.6 g.) is cooled to 20° and 28.2 cc. 98% HCO_2H added portionwise followed by 13 cc. 36% $HCHO$ solution, the mixture warmed to room temperature, heated 17 hrs. on a steam bath, poured into ice H_2O , made basic with 35% NaOH solution, extracted with ether, dried over K_2CO_3 , and distilled to get 21.2 g. 3-(benzylmethylamino)tropane (III), b0.3 135-8°, n25D 1.5416; picrate, m. 230-2° (from $HCONMe_2$); methiodide, m. 233.0-7.5° (decomposition). I (42 g.), 52.5 cc. 5.82N $MeNH_2$ in MeOH, 1.5 g. PtO_2 , and 100 ml. MeOH treated similarly yield 38.3 g. 3-methylaminotropane (IV), b23 109-10°, n25D 1.4934. When 15.2 g. IV, 12.6 g. $PhCH_2Cl$, and 13.8 g. K_2CO_3 in 100 cc. PhMe are heated 4 hrs. under reflux and 10% K_2CO_3 solution then added, three layers are formed. The bottom (aqueous) layer is discarded; the top (PhMe) layer is distilled to dryness, the residue dissolved in ether, filtered, and the filtrate distilled to get 5.6 g. III, b0.8 130-6°. The middle layer is taken up in $CHCl_3$, washed with H_2O , and the $CHCl_3$ distilled, ether added to an EtOH solution of the residue, and the solid (3.7 g.) separated and recrystd. from EtOH-ether to obtain the 8-benzochloride of III (V), m. 224.0-5.5° (decomposition); 8-(4-nitrobenzobromide) (VI), m. 220-3° (decomposition); 8-(4-chlorobenzochloride) (VII), m. 226-8° (decomposition); 8-(3,4-dichlorobenzochloride) (VIII), m. 232-5° (decomposition); 8-(p-methoxybenzochloride); 8-(p-methylbenzochloride). 3-(4-Chlorobenzylamino)tropane (IX), b0.2 135-53°; picrate, m. 185-7°. 3-(2-Phenylethylamino)-, 3-(3-phenylpropylamino)-, and 3-(2-phenylpropylamino)tropane are prepared by analogous methods. IX is heated with 1 molar equivalent $PhNCS$ to obtain the phenylthiureide, m. 130-2°. Replacement of I in the synthesis of IX with pseudopelletierine gives 3-(4-chlorobenzylamino)-9-methylgranatanine. IX (18.0 g.), 15 ml. 98% HCO_2H , and 6.85 ml. 37% $HCHO$ solution yield 12.4 g.

3-[(4-chlorobenzyl)methylamino]tropane (X), b0.3 140°; 8-methiodide (XI), m. 255-6° (decomposition); 8-methobromide, m. 261-3° (decomposition); 8-(4-nitrobenzobromide), m. 210-12° (decomposition). X, b0.1-0.2 144-6°, n_{25D} 1.5483, and its 8-(4-chlorobenzochloride) (XII), m. 202.5-205° (decomposition), are prepared by the method used for III and V. The 8-(3,4-dichlorobenzochloride) of XII, m. 200-3° (decomposition); 8-(2-hydroxyethobromide), m. 219-21°. A mixture of 50 g. 4-Et₂NC₆H₄CH₂NH₂ and 200 ml. 12% NH₃ in MeOH is hydrogenated (Raney Ni) 3 hrs. at 21-2° at an initial pressure of 890 lbs. per sq. in., filtered, distilled, and redistd. to obtain 23.2 g. 4-diethylaminobenzylamine (XIII), b0.1 122-8°, n_{25D} 1.5592. Hydrogenation of 19.0 g. I, 23.2 g. XIII, and 1 g. PtO₂ in 200 ml. absolute EtOH as before, solution of the crude product in absolute EtOH, and addition of excess alc. HCl give 21.5 g. 3-(4-diethylaminobenzylamino)tropane trihydrochloride dihydrate, m. 195° (decomposition); picrate of free base, m. 185° (decomposition). The phenylthiureide m. 145-7°; 8-methiodide (XIV), m. 240-5° (decomposition); 8-(4-chlorobenzochloride) (XV), m. 208-11° (decomposition); 8-(3,4-dichlorobenzochloride), m. 200-3° (decomposition); 8-(4-nitrobenzobromide), m. 189-91°. 3-(Benzylacetylaminotropane is prepared by treating II with Ac₂O followed by hydrolysis; reduction with LiAlH₄ yields 3(benzylethylamino)tropane. A solution of 36.2 g. 2,5-diethoxytetrahydrofuran in 240 cc. H₂O containing 0.6 ml. concentrated H₂SO₄ is warmed 15 min. on a steam bath, cooled, and added to a solution of 97 g. CO(CH₂CO₂H)₂, 146 NaOAc.3H₂O, and 27 PhNH₂ in 3.5 l. H₂O. After standing overnight, the solid is collected, dissolved in one 1.5% aqueous HCl at 60°, cooled, made alkaline with NH₃, and the product recrystd. from dilute MeOH to obtain 11.4 g. 8-phenylnortropanone (XVI), m. 107-9°; hydrogenation of a mixture of XVI, PhCH₂NH₂, and PtO₂ in EtOH gives 3-benzylamino-8-phenylnortropanone. V, VI, VII, VIII, XI, and XII are 60, 54, 74, 128, 30, and 100% as effective, resp., as hexamethylenebis(trimethylammonium bromide) in blockade of the sympathetic ganglia when measured by the carotid occlusion test in dogs. X, XIV, and XV are similarly 35, 26, and 210% as effective, resp., in cats.

IT 102552-20-5P, Nortropane, 3-benzylamino-8-phenyl-
 RL: PREP (Preparation)
 (preparation of)
 RN 102552-20-5 CAPLUS
 CN Nortropane, 3-benzylamino-8-phenyl- (6CI) (CA INDEX NAME)



L3 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1957:86038 CAPLUS
 DOCUMENT NUMBER: 51:86038
 ORIGINAL REFERENCE NO.: 51:15607c-i,15608a-i,15609a-h
 TITLE: Tertiary amino-substituted compounds of the tropane and granatanine series
 PATENT ASSIGNEE(S): Sterling Drug Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 762256		19561128	GB	

AB Tertiary amino substituted tropanes, granatanines, and their salts are prepared 3-Tropanone (30 g.), 24 g. 2-diethylaminoethylamine, 1.2 g. PtO₂, and 50 ml. EtOH is shaken in 50 lb./sq. in. H 2.5 hrs., the product filtered, the filtrate concentrated, and distilled to give 33.2 g. 3-(2-diethylaminoethylamino)tropane, b₅ 111-15°; picrate, m. 163.5-6° (from aqueous EtOH); trihydrochloride monohydrate, m. 267-71° (from 95% EtOH, MeOH); bismethiodide, m. 269° (from dilute MeOH) (decomposition). To 59 g. 3-[(2-diethylaminoethyl)amino]tropane cooled to -40° is added 54 ml. 100% HCO₂H followed by 24.6 ml. 36% HCHO, the mixture heated to 100° 16 hrs., treated with 35% NaOH, extracted with Et₂O, and then distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropane, b-1.0 120-3°, n_D25 1.4871. Similarly the following compds. are prepared: 3-[(2-diethylaminoethyl)amino]tropane bismethobromide, m. 289-90° (from MeOH) (decomposition); 3-[(2-diethylaminoethyl) methylamino]tropane trihydrobromide, m. 140° (from MeOH); 3-[(2-dimethylaminoethyl)amino]tropane, b_{0.5} 101.5-3°, n_D25 1.4880; 3-[(2-dimethylaminoethyl)methylamino]tropane, b_{1.2} 104-7°, n_D25 1.4900-9, m. 238-41° (decomposition); 3-[3-(1-piperidyl)propylamino]tropane, b_{0.2} 141.8-°, n_D25 1.5057; 3-{[3-(1-piperidyl)propyl]methylamino}tropane bisethiodide, m. 222-33°; 3-{[3-(1-piperidyl)propyl]methylamino}tropane trismethiodide, m. 207-14°; 3-[2-(1-piperidyl)ethylamino]tropane, b_{0.5} 132-3°; 3-[2-(1-piperidyl)ethylamino]tropane trihydrochloride, m. 275-7°; 3-[2-(1-piperidyl)ethylamino]tropane bis-methiodide, m. 293°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane, b_{0.07} 118.5-26°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane trihydrobromide, m. 220-4.5°; 3-{[2-(1-piperidyl)ethyl]methylamino}tropane bismethiodide, m. 259-60°; 3-{[2-(1-piperidyl)ethyl] methylamino}tropane bisethiodide, m. 215-19°; 3-[3-(1-pyrrolidyl)propylamino]tropane, b_{0.05} 140-4°; 3-{[3-(1-pyrrolidyl)propyl]methylamino}tropane, b_{0.2} 129-31°, n_D25 1.5031-40; 3-{[3-(1-pyrrolidyl)propyl]methylamino}tropane bismethiodide, m. 226-8°; 3-[2-(1-pyrrolidyl)ethylamino]tropane, b_{0.5} 130-5°; 3-[2-(1-pyrrolidyl)ethylamino]tropane bismethiodide, m. 290-3° (decomposition); 3-{[2-(1-pyrrolidyl)ethyl]methylamino}tropane, b_{0.3} 122-4°, n_D25 1.5055-60; 3-{[2-(1-pyrrolidyl)ethyl]methylamino}tropane bismethiodide, m. 205-20°; 3-[4-(1-pyrrolidyl)butylamino]tropane, b_{0.3} 142-8°, n_D25 1.5038-41; 3-{[4-(1-pyrrolidyl)butyl]methylamino}tropane, b_{0.2} 138-40°, n_D25.5 1.5029; 3-[2-(4-morpholinylethylamino]tropane, b_{0.4} 133-5°, n_D25 1.5066;

3-[2-(4-morpholinylethylamino)]tropane trihydrochloride, m. 245-9° (with decomposition); 3-[2-(4-morpholinyl)ethylamino]tropane bismethiodide, m. 264.5-5° (decomposition); 3-[[2-(4-morpholinyl)ethyl]methylamino]tropane, b0.1 124-30°, nD25 1.5079-83; 3-[[2-(4-morpholinyl)ethyl]methylamino]tropane trihydrobromide, m. 252-4° (decomposition); 3-[[2-(4-morpholinyl)ethyl]methylamino]tropane bismethiodide, m. 218-20°; 3-(3-dimethylaminopropylamino) tropane, b1.7 112-14°, nD24 1.4990 (tripicrate, m. 230°); 3-[(3-dimethylaminopropyl)methylamino]tropane, b0.5 106-12°, nD26 1.4885-8 [picrate, m. 231° (decomposition)]; 3-(3-diethylaminopropylamino)tropane, b0.1 120-5°, nD25 1.4862 [picrate, m. 212° (decomposition)]; 3-[(3-diethylaminopropyl)methylamino]tropane, b0.1 120-3°, nD25 1.4870; 3-[(3-diethylaminopropyl)methylamino]tropane bismethiodide, m. 222-7°.

Tropine (60 g.), 150 ml. PhMe, and 9.2 g. Na is refluxed 4 hrs., then 3 more hrs. with 42.8 g. 2-dimethylaminoethyl chloride in 50 ml. PhMe, aqueous MeOH added to the cooled product, and the organic layer separated,

concentrated, and

distilled to yield 17.3 g. 3-(2-diethylaminoethoxy)tropane, b0.9 85-0.5°, nD25 1.4836; bisperchlorate, m. 243-6° (from aqueous AcOH); bismethiodide, m. 314-5° (from MeOH) (decomposition). Similarly, the following compds. are prepared: 3-(2-diethylaminoethoxy)tropane, b0.07 101°, nD25 1.4758; 3-(2-diethylaminoethoxy)tropane bismethiodide, m. 301-2° (decomposition); 3-[2-(1-piperidyl)ethoxy]tropane, b0.07 106-9°; 3-[2-(1-piperidyl)ethoxy]tropane bismethiodide, m. above 305°; 3-[3-(1-piperidyl)propoxy]tropane, b0.1 115°; 3-[3-(1-piperidyl)propoxy]tropane bismethiodide, m. above 305°; 3-[2-(1-pyrrolidyl)ethoxy]tropane, b2.8 134°, nD25 1.4932; 3-[2-(1-pyrrolidyl)ethoxy]tropane bismethiodide, m. 313-4°; 3-(2-diethylaminoethoxy)pseudotropine, b0.25 109-12°, nD25 1.4775; 3-(2-diethylaminoethoxy)pseudotropine bismethiodide, m. 307-8° (decomposition); 3-(3-diethylaminopropoxy)tropane, b0.2 94-6°; 3-(3-diethylaminopropoxy)tropane bismethiodide, m. 300° (decomposition). 3-(2-Diethylaminoethylmercapto)tropane can be prepared by heating 3-bromotropine with 3-diethylaminoethylmercaptan in NaOH solution 1-Methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 264-7° (from H2O) (decomposition). Similarly the following compds. are prepared: 3-(2-phenylmethylaminoethylamino)tropane, b0.1 167-73°; 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.3 170-2°; 3-(2-phenylethylaminoethylamino)tropane, b0.6 174-7°; 3-(2-phenylethylaminoethylamino)tropane 8-methiodide, m. 226-8° (decomposition); 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.5 174-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 269-71°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine 8-methiodide, m. 235-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethobromide, m. 262-2.5° (decomposition).

2,5-Diethoxytetrahydrofuran (160 g.), 150 ml. H2O, and 0.13 ml. concentrated

HCl

stirred at 48-50° 2 hrs., cooled to 25°, 202 g. di-Et acetonedicarboxylate followed by 100 ml. H2O and 107 g. PhCH2NH2.HCl added, the mixture stirred overnight, treated with 250 ml. HCl, and heated to 103° to remove H2O, the residue filtered off, the filtrate made basic with 250 ml. 35% NaOH, 500 g. K2CO3 added, and extracted 3 times with Et2O gave 102 g. 8-benzyl-nortropanone, b0.4 134-7°, nD25 1.5562. Similarly are prepared: 3-(2-diethylaminoethylamino)-8-benzyl-nortropane, b0.25 161-8°, nD25 1.5235; 3-(2-diethylaminoethylamino)-8-

benzyl nortropane trihydrochloride, m. 264-6° (decomposition); 3-(2-diethylaminoethylamino)-8-benzyl nortropane bismethiodide, m. 255-7°; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl) nortropane trihydrochloride, m. 277-8° (decomposition); 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl) nortropane bismethiodide, m. 229-30°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl) nortropane trihydrochloride, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl) nortropane bismethiodide, m. 226-8°; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl) nortropane trihydrochloride, m. 275-6° (decomposition); 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl) tropane bismethiodide, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl) nortropane trihydrochloride, m. 273-5°; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl) nortropane; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl) nortropane bismethiodide, m. 232-4°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl) nortropane trihydrochloride, m. 248-51°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl) nortropane bismethiodide, m. 218.5-21.5°; 3-(2-diethylaminoethylamino)-8-phenyl nortropane; 3-(2-diethylaminoethyl)methylamino-8-phenyl nortropane. Hydrated pseudopelletierine (29.8 g.), 26 g. 2-(1-piperidyl)ethylamine, 600 mg. ZnCl₂, and 150 ml. C₆H₅CH₃ refluxed 64 hrs. using a separator to collect the H₂O formed, the product cooled, washed with 50 ml. saturated K₂CO₃

solution,

and the aqueous layer extracted with 4 50-ml. portions of C₆H₆ yielded 27.8 g. 3-2-(1-piperidyl)ethylimino-9-methylgranatanine (II), b₁ 164-76°, n_D²⁵ 1.5235. To 27.8 g. II in 40 g. 4-methyl-2-pentanol is added slowly 9.2 g. Na in 200 ml. PhMe, the mixture refluxed 0.5 hr., 30 ml. H₂O added, cooled, the aqueous layer saturated with K₂CO₃, extracted with 3 100-ml.

portions of

PhMe, the PhMe layers concentrated, dissolved in 50 ml. MeOH, 15 g. phenyl isothiocyanate stirred in, and the precipitate (34.4 g.) filtered off and recrystd. from AcOEt. By fractional precipitation from MeOH 2 isomers of 1-2-(1-piperidyl)ethyl-1-3-(9-methyl)granatanyl-3-phenylthiourea, isomer A, m. 174.5-6° (prisms from AcOEt), and isomer B, 173-4.5° (needles) are obtained. Also prepared were: 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine trihydrochloride (from isomer A), m. 285-7° (decomposition); 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine trihydrochloride (from isomer B), m. 276° (decomposition); 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea, m. 170.5-2°; 3-(2-diethylaminoethylimino)tropane, b_{0.6} 117-31°; 3-(2-diethylaminoethylamino)tropane; 1-(2-diethylaminoethyl)-1-(3-pseudotropanyl)-3-phenylthiourea, m. 138-9.5°; 3-(2-diethylaminoethylamino)pseudotropane trihydrochloride, m. 276° (decomposition); 3-(2-diethylaminoethylamino)pseudotropane bismethiodide, m. 279-81° (MeOH); 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine, b₂ 155-7°, n_D²⁵ 1.5102; 1-[2-(1-pyrrolidyl)ethyl]-1-[3-(9-methyl)granatanyl]-3-phenylthiourea, m. 173-4°; 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine bismethiodide, m. 278° (decomposition); 3-(2-diethylaminoethylamino)-9-methylgranatanine, b_{0.6} 128-30°, n_D²⁵ 1.4920; 1-(2-diethylaminoethyl)-1-(9-

methylgranatanyl)-3-phenylthiourea, isomer B, m. 188-90°;
 1-(2-diethylaminoethyl)-1-(9-methylgranatanyl)-3-phenylthiourea, isomer A,
 m. 135-6°; 3-(2-diethylaminoethylamino)-9-methylgranatanine
 trihydrochloride, isomer A, m. 278° (decomposition) [trihydrochloride of
 isomer B, m. 185°; bismethiodide of isomer A, m. 277-9°
 (decomposition)];

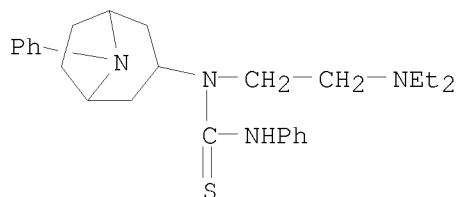
1-(2-diethylaminoethyl)-1-{3-[8-(2-chlorobenzyl)nortropanyl]}-
 3-phenylthiourea, m. 124-6°; 1-(2-diethylaminoethyl)-1-[3-(8-
 phenyl)nortropanyl]-3-phenylthiourea, m. 161-3°.
 3-(2-Diethylaminoethylamino)tropane (4.0 g.) treated with 1.7 ml. allyl
 isothiocyanate yielded 3.6 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-
 allylthiourea, m. 97-100°. Similarly the following compds. are
 prepared: 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-ethylthiourea, m.
 122-4°; 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-(4-
 ethoxyphenyl)thiourea, m. 160-1°; 1-(2-diethylaminoethyl)-1-[3-(8-
 benzyl)nortropanyl]-3-phenylthiourea, m. 138-9°;
 1-(2-diethylaminoethyl)-1-{3[8-(3,4-methylenedioxybenzyl)]nortropanyl}-3-
 phenylthiourea, m. 148-9°; 3-[(2-diethylaminoethyl)acetylaminotro-
 pane, b0.09 142-4°, nD25 1.4980 (picrate, m. 190-200°) (from
 EtOH); 3-[(2-diethylaminoethyl)ethylaminotropane, b2 142°, nD25
 1.4845 (bismethiodide, m. 230-1°) (decomposition); 3-[(2-
 diethylaminoethyl)ethylaminotropane bismethiodide, m. 226°
 (decomposition); 3-[(2-diethylaminoethyl)propionylaminotropane, b0.5
 160°, nD28 1.4940-5 (picrate, m. 173-6°) (from aqueous HCONMe2);
 3-[(2-diethylaminoethyl)propylaminotropane, b0.1 119-26°, nD28
 1.4835 [picrate, m. 223° (decomposition); bismethiodide, m.
 203-9° (decomposition)]; 3-[(2-diethylaminoethyl)butyrylaminotropane,
 b0.7 162-6°, nD25 1.4935 (picrate, m. 194-6°);
 3-[(2-diethylaminoethyl)butylaminotropane, b0.1 125-30°, nD25
 1.4839 [picrate, m. 208-10° (decomposition)]; 3-[(2-
 diethylaminoethyl)acetylaminotropane, b0.2 183-98°,
 nD28 1.5470; 3-[(2-diethylaminoethyl)ethylaminotropane, b0.9
 180-4°, nD30 1.5370; 3-[(2-phenylethylaminoethyl)formylaminotropan-
 e, b0.1-0.2 200-7°; 3-{[2-(1-pyrrolidyl)ethyl]formylaminotropane,
 b0.9 166-72°, nD25 1.5131 (picrate, m. 192-4°);
 3-[2-phenylethylaminoethyl)methylaminotropane, b1.6 182-7°, nD24
 1.5518.

IT 123935-68-2

(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
 (6CI) (CA INDEX NAME)



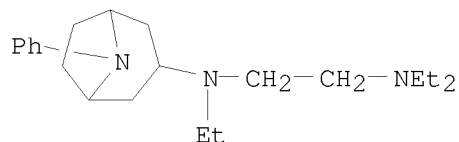
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 diethylaminoethyl)methylamino]-8-phenyl- 102709-02-4P,
 Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- 110147-72-3P

10/513699

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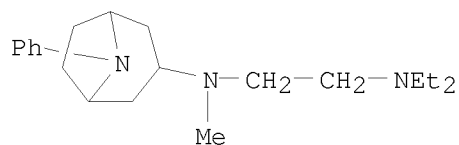
RN 102457-13-6 CAPLUS

CN Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- (6CI) (CA INDEX NAME)



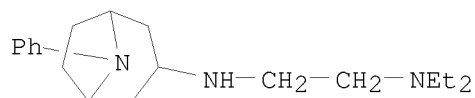
RN 102463-23-0 CAPLUS

CN Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- (6CI) (CA INDEX NAME)



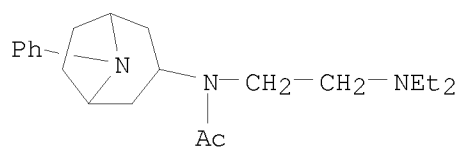
RN 102709-02-4 CAPLUS

CN Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 110147-72-3 CAPLUS

CN Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- (6CI) (CA INDEX NAME)



L3 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1957:86037 CAPLUS
 DOCUMENT NUMBER: 51:86037
 ORIGINAL REFERENCE NO.: 51:15606g-i,15607a-c
 TITLE: Heterocyclic alcohol diammonio esters
 PATENT ASSIGNEE(S): Cutter Laboratories, Inc.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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GB 770581		19570320	GB 1955-8626	19550324

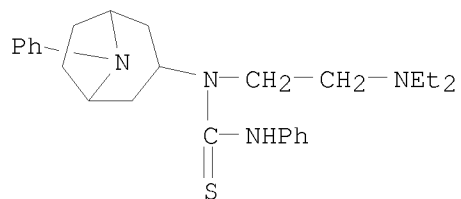
AB Esters containing two quaternary nitrogens, a trialkyl N being on the acid moiety and a heterocyclic N on the alcohol moiety are useful as hypotensor agents. Thus, to make 2-(1-ethylpiperidinium)ethyl 3-(trimethylammonium)propionate diiodide (I), 10.0 g. 1-ethyl-1-(2-hydroxyethyl)piperidinium iodide (II) was first acylated 1 hr. with 26 g. I(CH₂)₂COCl (III) on a steam bath. This product was washed with Et₂O, MeOH and then Et₂O to yield a residue which was dissolved in an MeOH-dioxane (10 ml.:25 ml.) and mixed with 2.1 g. Me₃N in 16 ml. dioxane. After 3 days, 10.6 g. I, m. 169-71° (from MeOH), separated. Directions are given for similar reactions to yield the following 2-(substituted-ethyl)-3-(trimethylammonium)propionate diiodides (substituent on C-2 of ethyl, yield and m.p., crystallization solvent given): 1-methylpiperidinium, 52%, 170-1°, MeOH-Et₂O (IV); 1-methylpyrrolidinium, 81%, 190°, IV; 4-methylmorpholinium, 61%, 188-90°, MeOH. An alternative procedure was represented by refluxing 10 g. 2-(4-methyl-1-piperidyl)-2-propyl 3-(dimethylamino)propionate (V), in 500 ml. Me₂CO 1 hr. with 20 g. MeI. Upon cooling, the mixture yielded 16.3 g. 2-(1,4-dimethylpiperidinium)-2-propyl 3-(trimethylammonium)propionate diiodide (VA), m. 170-2° (from wet Me₂CO). II was prepared in 60% yield by refluxing 24 hrs. 13.5 g. 2-iodoethanol in 50 ml. MeOH with 9.0 g. 1-ethylpiperidine. The oily II which separated on cooling slowly solidified. Crystallization of this solid from Me₂CO-MeOH (100 ml.:50 ml.) yielded 10.3 g. II, m. 240°. 1-(2-hydroxyethyl)-1-methylpiperidinium iodide, m. 235-8°, was similarly prepared in 93% yield. Equimolar quantities of 4-methylpiperidine and propylene oxide, when refluxed 4.5 hrs. and distilled, yielded 80% 1-(4-methyl-1-piperidyl)-2-propanol (VI), b. 210-12°. VI was slowly added to 1 mole acrylyl chloride in C₆H₆ and this mixture then refluxed 2.5 hrs. The C₆H₆ solution, after washing with cold saturated NaCl solution and excess Na₂CO₃ solution, yielded 69% 2-(4-methyl-1-piperidyl)-2-propyl acrylate (VII), b₂. 5 85°. When 1 mole gaseous Me₂NH was passed into cold VII and this mixture held 17 days at room temperature (sealed tube), distillation (93-8° at 1.5 mm.) yielded V containing about 20% VII, satisfactory for producing VA. III (b₁ 75-80°) was prepared in 75% yield by refluxing I(CH₂)₂CO₂H (36 g.) with 14 ml. PCl₃ 5 hrs. and distilling. Using an ion exchange column (Cl form), I was converted to its dichloride, m. 200-1°. The dinitrate, m. 142°, and the dibitartrate, m. 123-6°, of I were prepared from I and the appropriate Ag salt. Picric acid and I yielded I dipicrate, m. 182-3°. In most examples, analyses are given.

IT 123935-68-2
 (Derived from data in the 6th Collective Formula Index (1957-1961))

10/513699

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-
(6CI) (CA INDEX NAME)



<12/04/2007>

Erich Leese

10/513699

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(FILE 'HOME' ENTERED AT 20:25:33 ON 22 FEB 2008)

FILE 'REGISTRY' ENTERED AT 20:25:48 ON 22 FEB 2008

L1 STRUCTURE UPLOADED

L2 214 S L1 FULL

FILE 'CAPLUS' ENTERED AT 20:26:52 ON 22 FEB 2008

L3 19 S L2 FULL

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

104.51

283.54

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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